An analysis of sociodemographic, dietary and environmental determinants of allergic rhinitis and atopic eczema symptoms among adolescents in Cape Town, South Africa: findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three Study

Astrid Chrisilda Dearham

MBChB (University of Cape Town)

Dissertation presented for the degree of Masters in Medicine (MMed) (Public Health)

School of Public Health and Family Medicine

University of Cape Town

April 2011

TABLE OF CONTENTS

I dedicate this dissertation to my late father, Isaac Dearham, as well as my mother, Lenore. I am privileged to always have the incredible support, faith and patience of my sister, Vania, my partner Kurt, other family members and close friends during this process and everything else I do.

DECLARATION

The work presented in this report represents analyses of data collected as part of a larger international multicentre collaborative study, the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. Under the supervision of Professor R.E. Ehrlich, the role of the author was restricted to the data analyses of the specified conditions and the documentation of findings, presented as Parts of this dissertation. Therefore, the analyses presented in this dissertation are the original work of the author and have not been submitted for other degree purposes, or publication before. Where the work of others has been used (whether it has been quoted verbatim or paraphrased or referred to) it has been attributed and acknowledged using the Harvard referencing convention.

Signature : _____

Date : _____

ACKNOWLEDGEMENTS

Firstly, I would like to convey my heartfelt gratitude to my supervisor Professor Rodney Ehrlich. Your wisdom, guidance and attention to detail have been humbling and invaluable lessons. To both Professor Rodney Ehrlich and Professor Heather Zar, thank you for the opportunity to use the ISAAC Phase Three data for my dissertation. To Anna Grimsrud, thank you for the ad hoc statistical advice you have provided.

As mentioned by authors who have used the ISAAC data of the Cape Town centre, once again a word of appreciation is extended to the field researchers, the Dept. of Education in the Western Cape, the school principals, teachers, children and parents for participating. The study was supported by a grant from the Medical Research Council, South Africa, an AstraZeneca Respiratory fellowship awarded by the South African Thoracic Society (Heather Zar), and sponsorship from the following pharmaceutical companies: AstraZeneca, Boehringer-Ingelheim, 3M and Schering-Plough. We thank the International ISAAC centre, New Zealand for a start-up grant and for advice and support.

STRUCTURE OF THE DISSERTATION

An abstract of the study is first presented. Thereafter there are 3 parts to the dissertation.

Part A is the protocol that outlines the justification for the study, the methods and analyses as well as the ethical implications.

Part B presents the findings of the literature review that was conducted. Current evidence on the validation of the rhinitis and eczema ISAAC questionnaires as well as the relevant sociodemographic, dietary and environmental exposures of the conditions individually and together, is appraised. The influences of socioeconomic status and "upward mobility" are also reviewed.

Part C concludes the dissertation in the format of a submission to the Journal of Allergy and Clinical Medicine. The format deviates from the journal instructions in that line numbers have not been included and, to maintain consistency between the Parts, the Harvard referencing convention – and not Vancouver - has been used.

The key results of logistic regression analyses are presented for the outcomes of allergic rhinitis and atopic eczema. Where possible, these are compared to the previous findings for the outcome of wheeze.

References and appendices are at the end of the dissertation. Appendix I includes the "Instructions to authors" as provided by the *Journal of Allergy and Clinical Immunology* as well as the consent forms and questionnaires. Appendix II (the Online Repository for the journal) includes the full outputs of analyses as well as additional results that were not presented in the other thesis parts.

ABSTRACT

Background

Most analyses of International Study of Asthma and Allergies in Childhood (ISAAC) data in developing countries have suggested an increase over time in 12-month prevalence of rhinitis and eczema symptoms amongst adolescents. Analysis of the Cape Town Phase Three data for the determinants of allergic rhinitis and atopic eczema symptoms has not yet been conducted.

Objective

To measure the sociodemographic, dietary and environmental risk factors of allergic rhinitis and atopic eczema symptoms amongst adolescents of the Cape Town centre of the ISAAC Phase Three study.

Methods

A cross-sectional study design using written questionnaires was performed in 2002. The study population included 5, 037 adolescents who attended 54 schools. Logistic regression with stepwise model-building was done. The findings were compared to the findings of wheeze symptoms that was also analysed using the same dataset.

Results

Totals of 20.7% (1, 043) and 13.3% (670) of the respondents reported experiencing symptoms of allergic rhinitis and atopic eczema respectively. 212 (4.2%) of respondents reported that rhinitis symptoms had a significant impact on their daily activities. Only 244 (4.8%) respondents reported that they had experienced comorbid symptoms. In general, findings were suggestive of different social class gradients: a higher SES associated with allergic rhinitis (and wheeze) was protective of atopic eczema. Male gender was protective

for both outcomes. Paracetamol use at least once a month was positively associated with all 3 outcomes. A household member with TB was a predictor for both allergic outcomes. Cereal and maize consumption 3 or more times (versus less often or never) a week were predictors of both outcomes. “Commuting” students (from low SES areas to high SES schools) had 1.3 odds for the outcome of allergic rhinitis compared to those from the same low SES area but who attended low SES schools (OR 1.33; 95% CI 0.78-2.29). For the outcome of atopic eczema, the findings are suggestive of a protective effect; although to a lesser degree than the students from higher SES areas.

Conclusion

This is the first analysis of the Cape Town ISAAC data that has compared the determinants of allergic rhinitis and atopic eczema to previously analysed wheeze symptoms. The contribution of social class to allergic disease in South Africa is suggestive from these findings. Although frequent paracetamol use was associated with all outcomes and biologically plausible mechanisms are present, this study was unable to exclude reverse causation. The role of gender and TB in allergic disease requires further research.

PARTS AND SUBHEADINGS

LIST OF FIGURES

LIST OF TABLES

Part A: Protocol

I. INTRODUCTION

1. Problem

The increase in allergic disorders amongst children has become a focal area for research and debate, especially around the contribution of dietary and environmental determinants. Intermittent research has been stimulated by the use of standardized instruments in The International Study of Asthma and Allergies in Childhood (ISAAC).

ISAAC is a multicentre collaborative study that was first undertaken in 1992 to measure the prevalence of three allergic disorders through self-reported symptoms: asthma, rhinoconjunctivitis and eczema in school goers. Three phases were conducted from 1992 onwards and the application of a standardised method by different centres in studies across the world has ensured that results can be compared (Asher 1995).

Phase One studies were conducted between 1992 and 1995 in 56 countries and documented the baseline distribution of these three allergic conditions across all the centres participating in the study (Asher 1995; 1998).

Phase Two was conducted in 22 countries, although not in South Africa, and aimed to provide further information on risk factors by conducting physical examinations and laboratory tests on the adolescents (Weiland 2004).

Phase Three was conducted from 2002 onwards in 106 countries (Ellwood 2005). The illustration of a "world map" - as well as the documentation of trends in the prevalence of the three disorders - is now possible.

Most analyses of ISAAC Phase Three data in developing countries have demonstrated substantial increases in the 12-month prevalences of all three allergic conditions. According to Odhiambo et al. (2009), "Trends in eczema symptoms... indicate that the prevalence of eczema is rising, especially in younger children, suggesting that environmental factors could be playing a key role in determining disease expression." A similar increase in the prevalence of rhinitis symptoms has been suggested (Ait-Khaled 2009; Bjorksten 2008).

Asthma prevalence, its severity and predictors of risk have previously been analysed based on the ISAAC Phase One and Phase Three studies in Cape Town, South Africa (Poyser 2002; Graham 2002; Mahlati 2007).

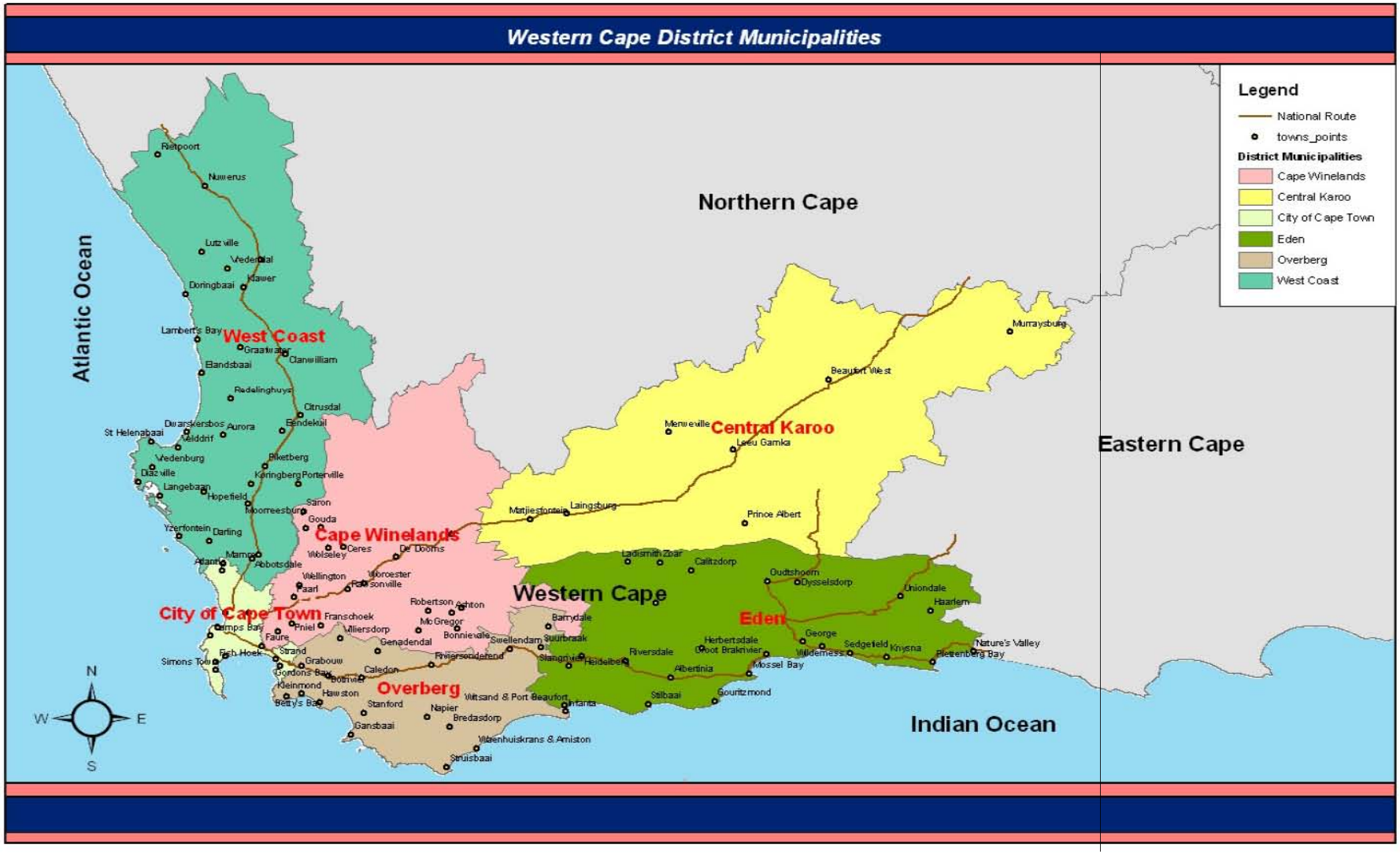
Two reports have documented the prevalence of allergic rhinitis and atopic eczema in Cape Town. Using the ISAAC Phase One dataset, Mercer et al. (2004) analysed the prevalence of allergic rhinitis and atopic eczema symptoms by socioeconomic status (SES). The second report was written by Zar et al. (2007) who assessed trends in the symptoms of all three allergic conditions by using both ISAAC Phase One and Three data. Further analysis of the ISAAC Phase Three data in Cape Town for the predictors of risk of allergic rhinitis and eczema has not yet been conducted. Therefore, an opportunity arose to contribute to knowledge of the significant sociodemographic, dietary and environmental risk factors for allergic rhinitis and eczema by using the ISAAC Phase Three data.

Background to the Western Cape province and Cape Town district

The Western Cape province is located in the south west area of the Republic of South Africa (Figure 1). According to the Census survey of 2001 (Pretoria: Statistics South Africa 2005), there were 4,524,335 persons in the Western Cape (10.1% of the population of South Africa) at that point in time. There were 5 district rural municipalities. The City of Cape Town was classified as a metropolitan municipality. The boundaries of the rural districts have since changed.

The Census 2001 revealed the following socidemographic findings. Afrikaans was the most frequently spoken home language in the province, followed by English and then Xhosa. Although the City of Cape Town – the study centre for ISAAC in the country - covers the smallest surface area, it accommodated approximately 66% of the population in 2001. Amongst those aged 13 to 14 years – the age group of the ISAAC population in the Cape Town centre, approximately 95% were attending an educational institution. In both Censuses of 1996 and 2001 amongst those aged 15 to 65 years in the province, the African and Coloured population groups had higher proportions of unemployment than other groups. Lastly, 77% (920 000) of households lived in formal housing structures while 15.8% (190 000) lived in informal structures such as shacks. A marker of social mobility is the proportion of African-headed households who live in formal dwellings. This had increased from 31.9% in 1996 to 45.4% in 2001 (Pretoria: Statistics South Africa 2005).

Figure 1 Map of Western Cape District Municipalities (source: Annual Performance Plan 2010)



2. Justification for further research

Prevalence trend of allergic rhinitis and eczema symptoms

An analysis of ISAAC Phase One data in Cape Town demonstrated the 12-month prevalences of allergic rhinitis and atopic eczema symptoms to be 33.2% and 11.9% respectively (Mercer 2004), both higher than the worldwide Phase One medians that were reported (Strachan 1997; Williams 1999).

A follow-up study using the ISAAC Phase Three survey of 2002 by Zar et al. (2007) found that the lifetime prevalences of both allergic rhinitis and eczema symptoms had increased significantly from Phase One; the former from 37.6% (1995) to 49% (2002) while eczema increased from 9.6% (1995) to 16.7% (2002). The 12-month prevalences of both symptoms had also increased in both males and females.

Impact of allergic rhinitis and eczema symptoms

As with asthma, although the symptoms of allergic rhinitis and atopic eczema may have a minimal impact on routine activities, they may in some cases be distressing to the affected adolescent. In the comparison between ISAAC Phase One and Three, Zar et al. (2007) found that the reporting of both conditions, in their adverse impact on daily activities (for rhinitis) and night waking (for eczema) more than once a week, had increased. This was more substantial for rhinitis; in Phase One only 13% reported little impact on daily activities; in Phase Three this had increased to 26.2%. Moderate/severe impact increased from 9.3% to 11.6%. The direct and indirect effects (e.g. sleep deprivation and marital problems) and financial costs incurred by families who have a child with atopic eczema have been shown elsewhere to be considerable when compared to other chronic diagnoses such as diabetes (Su 1997).

Determinants of allergic rhinitis and eczema symptoms

The concept of the atopic march - when a child with eczema progresses to asthma and rhinitis in adulthood – is widely accepted (Bergmann 1998; Spergel 2003). However, this concept as well as the belief in the common causation of asthma, eczema and rhinitis has been challenged by Williams et al. (2006; 2008). These authors suggest that not only may the "march" not be as straightforward as thought, but that the environmental risk factors may not be the same for the 3 allergic conditions.

A Cape Town Phase Three thesis analysis of asthma (Mahlati 2007) suggested that the presence of the following environmental exposures had associations with the reporting of current wheeze: maternal and respondent smoking, being overweight for age and exposure to wood smoke. Exercise at least once a week and paracetamol (acetaminophen) used at least once a month were also found to have positive associations with asthma.

Other environmental exposures such as truck traffic frequency and household smoking have been positively associated with not only asthma symptoms, but also those of rhinoconjunctivitis and eczema (Brunekeef 2009; Annesi-Maesano 2004). However, overall there appear to be a lack of consistency between the findings of studies conducted across the world with respect to these risk factors (Strachan 1998; Codispoti 2010).

The effect of paracetamol use on allergic disorders in children is particularly well researched (Cohet 2004; Beasley 2010; Asher 2010). Positive associations between paracetamol use and allergic outcomes have been demonstrated in most studies although the nature of the study designs has limited interpretation of the associations.

The influence of dietary factors such as starch, cereals, vegetables and seafood consumption on the symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema have been explored with inconsistent results worldwide (Ellwood 2001; Huang 2001; Chatzi 2009; Asher 2010). A protective dietary factor in one country may be a predictor for risk of disease in another.

Variation by SES and social mobility

The impact of the home environment (type of dwelling and overcrowding) and other proxy markers of SES such as maternal education for the risk and severity of allergic disease are important. The SES gradient is often positive. For example, a positive association was found between SES and the symptoms of rhinoconjunctivitis but not eczema in the Phase One Cape Town analysis (Mercer 2004). Mahlati (2007) also demonstrated a tertiary education of the mother to be one factor that consistently increased the odds of reporting wheeze symptoms and a diagnosis of asthma to be made greater. High parental education is also found to be a risk factor for diseases ever diagnosed by a physician as well as common cold symptoms in a study by du Prel et al. (2006).

A marker of social mobility was examined by Poyser et al. (2002) in an analysis of Phase One asthma prevalence by school type. Three groups of adolescents were examined; low SES adolescents attending low SES schools, high SES adolescents at high SES schools and low SES adolescents (mainly Xhosa-speaking adolescents from low income areas) at high SES schools. Different results were found for the written and video questionnaires. In the former, the highest prevalences of asthma and recent wheeze were found amongst the high SES adolescents at high SES schools; in other words the most “affluent” adolescents of the three strata. However, in the video questionnaire, the prevalence of asthma symptoms in the last 12 months based on a five step video sequence was considerably higher amongst the low SES adolescents attending low SES schools; i.e. the “commuting” adolescents.

After finding no significant association between urbanisation (duration of time in years in an urban area) and the prevalence of asthma symptoms, the authors suggested that upward mobility – demonstrated by the low SES adolescents commuting to attend schools outside their areas – might be a more relevant predictor of disease prevalence.

Mercer et al. (2004) also found that there were higher prevalences for both rhinitis and eczema conditions amongst students from the lowest SES areas who attended schools in

the highest SES areas. The Phase Three data have not been analysed using the above stratification.

In summary, a study of the Cape Town Phase Three data would be valuable for the following reasons: to establish whether associations of sociodemographic, dietary and environmental risk factors with the symptoms of rhinitis and eczema are similar to those found for asthma; to determine whether adolescents with both symptoms of allergic rhinitis and eczema have the same risk factors as those for each condition individually and to confirm whether Phase One social mobility differences in disease are present in the most recent dataset.

3. Research Aim

To investigate the prevalences of allergic rhinitis and atopic eczema symptoms (see definitions below) and their associations with sociodemographic, dietary and environmental risk factors in the 13 to 14 year old group of adolescents who were studied in the Cape Town, South Africa centre of the ISAAC Phase Three study in 2002.

4. Objectives

a. To measure and analyse risk factors associated with the reporting of allergic rhinitis and atopic eczema symptoms in a population of adolescents in Cape Town, South Africa using ISAAC Phase Three data.
b. To identify risk factors common to both conditions, as well as to current wheeze symptoms that was analysed by another researcher in 2007 using the same dataset.
c. To measure and analyse risk factors amongst those adolescents with both allergic rhinitis and atopic eczema (comorbid) symptoms.
d. To measure the influence of socioeconomic status (SES) and upward social mobility on these allergic symptoms.

II. METHODS

1. Definition of Terms

a. Allergic rhinoconjunctivitis ("allergic rhinitis"). This was defined by a positive answer to "Have you had problems with sneezing, or a runny, or blocked nose when you did not have a cold or the flu in the past 12 months?" and "In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?" (ISAAC manual; 1993).

b. Atopic eczema. Two questions were used to assess the prevalence of eczema: ""Have you ever had this itchy rash at any time in the past 12 months?" and "Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?" (ISAAC manual; 1993).

c. Race, language, residence and social class. According to Jones (2001), race is a social construct and a crude "proxy to measure social class, culture and genes." In South Africa, because of the segregation policies that were enforced and based on the perceived colour of one's skin during the Apartheid era, there has been a continuation of collecting data according to these groups since they determined access to health care, residence, education and employment. The racial categories were: "White" (persons of European descent), "Black" (also known as "Africans"), "Coloured" (persons of perceived "mixed" race) or "Indian" (persons of Asian descent). Africans, who were predominantly Xhosa-speaking and Coloured persons, were more likely to live in urban areas known as "townships" that, apart from overcrowding, did either not have basic amenities in place or had services that were of a lower standard than Whites. Because the time period in which the ISAAC data were collected was relatively shortly after the achievement of democracy in 1994, race and its associated language and residential variables still hold high potential validity to demonstrate social inequalities (Myer 2004). Three types of schools were

identified in the Cape Town study and classification has been based on previous historical segregation; those that were attended by predominantly Xhosa-speaking adolescents; those that were attended by predominantly Coloured adolescents and located in “Coloured areas” and lastly, those formerly White only schools situated in high SES areas. The last category of school was attended by adolescents from all areas after 1994 and is referred to as “integrated” schools.

d. Hygiene hypothesis. The hypothesis suggests that the higher rate of acquisition of allergic or autoimmune disease, or a higher prevalence of previously stable conditions in populations, may be attributable to a loss of protective immune factors that were previously induced by exposure to microbial agents in food and the environment. Clough et al. (2010) summarizes the hypothesis as “lower rates of exposure to certain kinds of allergens, bacteria and other microorganisms have had unintended, negative consequences for immune health”.

2. Study Design

In order to standardize the methodology to measure self- reported symptoms and diagnoses in 13 to 14 year old school children, a cross-sectional study design using standardized ISAAC written and video questionnaires was performed in 2002. The study also made use of two written questionnaires as well as a video-based questionnaire which were completed by the students.

3. Population and Sampling

3.1 Study Population

The study population in the ISAAC study included both male and female adolescents aged 13 and 14 years who attended schools in Cape Town.

3.2 Method of Sampling

Since the school was the primary sampling unit, the standardised ISAAC methodology required that a minimum of ten schools be included in each centre. A stratified random sampling strategy was based on a list of Cape Town-based schools provided by the local Department of Education. The decision to stratify according to the predominant racial group at the school (White/integrated, Coloured or Black) was informed by the previous political environment that legislated such racial descriptions. Schools were divided into these 3 strata and then randomly selected. ISAAC Phase Three also required that all adolescents aged 13 and 14 years from the selected schools be eligible whilst other ISAAC studies were adapted to include 6 and 7 year old children. In this study, adolescents in the two grades with the most 13 and 14 year olds in the schools were surveyed. To ensure that all eligible adolescents were included and that absenteeism was compensated for, each school was visited twice.

3.3 Sample size

The ISAAC methodology determined the sample size, which was calculated to be 3, 000 children, for the outcomes of wheeze, rhinitis or eczema (Asher 1995). The size was based on the more severe atopic disease than the prevalence of disease of any severity. This size would ensure a power of 95% to detect a significant difference in prevalence in two centres with true prevalences of 25% and 30% respectively at the 1% significance level; and 90% study power to detect a significant difference in prevalence of severe asthma between centres with true differences of 3% and 5% respectively at the 1% confidence level.

4. Measurement

4.1 Instrument

The ISAAC Phase Three methodology requires the use of the following three standardized and validated questionnaires (Appendices 1E to 1G) which are described in greater detail in the original papers (Ellwood 2005):

1. The core written questionnaire;
2. The environmental written questionnaire;
3. The video questionnaire

The *core written questionnaire* consists of demographic questions as well as those that pertain to the prevalence of the symptoms of allergic rhinitis and eczema.

The relevant questions to the intended analyses are listed below:

Rhinitis

1. Have you ever had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu?
2. In the past 12 months, have you ever had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu?
3. In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?
4. In the past 12 months, how much did this nose problem interfere with your daily activities?
5. Have you ever had hay fever?

Eczema

1. Have you ever had an itchy rash which was coming and going for at least six months?
2. Have you had this itchy rash at any time in the past 12 months?
3. Has this itchy rash at any time affected any of the following places? (Options provided)
4. Has this rash cleared completely at any time during the past 12 months?

5. In the past 12 months, how often, on average, have you been kept awake at night by this itchy rash?
6. Have you ever had eczema?

The *environmental questionnaire* was designed by the ISAAC Steering committee to provide information regarding dietary and environmental exposures. The ISAAC international centre did allow for the modification of the questionnaire either by excluding certain questions from the original questionnaire, or addition of questions on additional risk factors that are locally relevant.

All in all, one dietary risk factor and eleven environmental exposure questions were added for the Cape Town study. A question regarding maize was included as a dietary risk factor as maize was, and still is, part of the staple diet for many South Africans. The additional eleven environmental questions are listed below:

1. Do you smoke cigarettes?
2. Is your house damp or wet inside?
3. Has anyone in your household ever had TB?
4. Have you ever been treated for TB?
5. Do you have taps for running water in your house?
6. Do you have electricity in your house?
7. Do you have a TV in your house?
8. Type of home: House, Flat, Shack or Other
9. Number of people working in the household
10. Number of people not working in the household
11. Number of people sharing a room with the respondent at night

Since ISAAC questions of overcrowding, damp, access to tap water, fuel use and house type are both SES and environmental markers – and SES may be mediated through these variables - it has been decided for the purposes of this study to limit the sociodemographic determinants to language, gender, education, employment, and access to television in the house. The rest of the variables will be considered as environmental factors.

Lastly, the *video questionnaire* was included to reduce the language understanding and translation barriers that may be encountered with the written questionnaire. In the Western Cape province, Cape Town, there are three commonly used languages; English, Afrikaans and Xhosa. The direct translation of some of the terminology, for example “asthma”, is prone to misinterpretation. Hence, the video questionnaire was used to reduce the potential misinterpretation relating to asthma. However, there is no video questionnaire for the outcomes of allergic rhinitis and eczema

The following procedure for the questionnaire administration was recommended by the ISAAC Steering Committee (1993) i) The three questionnaires – the core written, the environmental and the video questionnaires – would be self-administered and the sequence to follow is to complete them in order all on the same day. ii) A facilitator would follow the standardised process and show the video at each school using the language that was the medium of instruction (Xhosa, English or Afrikaans).

III. ANALYSIS FOR THIS DISSERTATION

1. Data Analysis

A "stem and branch" question format was used in the core written questionnaire. For example, regarding rhinitis, "Have you ever had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu?" is a stem question, followed by "(if yes), In the past 12 months, have you ever had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu?" (branch question). Following a negative response to a stem question, the questionnaire prompts the participant to proceed to the next question.

Therefore, the coding for stem questions could either be "yes (1)" or "no (2)" or "9 (missing)" if the question was skipped by the respondent. Contradictory responses will be excluded from analyses. For branch questions, prevalence will be calculated using as the denominator the sample that answered both the stem and branch questions.

Analysis will be conducted according to the format of the question.

To address the objective of analysis of allergic rhinitis and eczema outcomes according to a potential "commuting status" marker for SES mobility, the following steps will be carried out:

a. The schools of the adolescents will be classified into either low SES or high SES based on the name and location of the school, as judged by the researcher.

b. The SES status of the adolescents will be based on the residential suburb as provided by the participant. Those adolescents residing in the lower SES areas but attending schools in affluent areas will be classified as "commuters". The comparison groups will be those adolescents residing in and attending schools located in the same area; that is, whether low SES or higher SES areas.

2. Statistical analysis

Stata version 11 (Stata Corporation) will be used to analyze the data.

The following data analyses will be undertaken:

a) One way frequency tables with measures of central tendency and dispersion will be used for the demographic profiling.

b) Two way frequency distribution tables will be used to cross tabulate categorical variables of interest.

c) Measures of central tendency (mean or median) and dispersion will also be used for numeric variables.

d) Bivariate analysis with the odds ratio (OR), 95% confidence interval and p value, will be conducted to measure associations between an exposure and the outcome variable/s of interest.

e) Multivariate logistic regression will be performed by fitting statistically significant predictors from the bivariate analyses and/or those of *a priori* relevance or interest against the outcome variables of interest.

f) Model checking will be done using the Pearson-goodness-of-fit statistic.

IV. ETHICS & COMMUNICATION

1. Ethics

Ethics approval for the 2002 ISAAC study was granted by the Research Ethics Committee of the University of Cape Town (*Ethics approval no. 203/2001*) (Appendix 1B). As part of the process, the Western Cape Department of Health and the appropriate school principals were approached for permission for the study; a letter with an opt-out clause was also sent to the parents/guardians of the selected adolescents (Appendix 1C and 1D).

2. Feed-back and Dissemination of this analysis

The findings will be submitted as part of the Master of Medicine (MMed): Public Health dissertation at the University of Cape Town. It will also be submitted in the appropriate format to a peer-reviewed journal. The findings will also be communicated to any special interest reference groups affiliated to the Western Cape Provincial Department of Health as well as the Maternal, Child and Women's Health Directorate within the Department of Health of the Provincial Government of the Western Cape.

Part B: Literature review

I. OBJECTIVES OF THE LITERATURE REVIEW

1. To summarize the literature on the validation of ISAAC instruments used to measure the prevalence of symptoms of allergic rhinitis and eczema.
2. To review the most pertinent sociodemographic, dietary and environmental risk factors associated with allergic rhinitis and eczema.
3. To review the influence of upward social mobility on the symptoms of allergic rhinitis and eczema.

II. REVIEW OF RELEVANT RESEARCH

1. To summarize the literature on the validation of ISAAC instruments used to measure the prevalence of the symptoms of allergic rhinitis and atopic eczema.

The International Study of Asthma and Allergies in Childhood (ISAAC) - a multicentre collaborative study - was undertaken to measure the prevalence of three allergic disorders through self-reported symptoms: asthma, allergic rhinoconjunctivitis and eczema in school goers. Since 1992, three Phases have been conducted worldwide (Asher 1995 and 1998; Weiland 2004; Ellwood 2005).

As with asthma, the core written questionnaire (one of three of the methods) was designed to assess the prevalence and severity of current allergic rhinitis and atopic eczema symptoms.

There have been concerns about the use of symptom-based questionnaires in ISAAC; particularly with the lack of a video component in rhinitis and eczema and the lack of a standardised physical examination in all three outcomes.

1.1 Eczema symptoms

In 2009, Flohr et al. used the Phase Two studies to compare the atopic eczema findings between the questionnaire and a physical skin examination for which a standardized protocol was used. Comparisons were done: i) at the level of the study centre to ascertain the validity of the questionnaire at a population level and, ii) at the level of the respondents to assess the questionnaire as a diagnostic tool.

The analysis was done on 30,358 children aged 8 to 12 years from 25 study centres in 18 countries. Ghana was the only African country that was included.

The authors found that in all but one study centre (Pichincha, Ecuador), flexural eczema prevalence based on physical examination (mean 3.9%) was lower than prevalence estimates that were derived from the questionnaire (9.4%). At a population level, the correlation between the ISAAC Phase Two questionnaire and examined eczema was high and was sensitive to differences in eczema severity ($r = 0.77$, $P < 0.001$). At an individual level, there were approximately 8% of cases of flexural eczema that were diagnosed on physical examination but not detected by questionnaire, which was not a concern. However, amongst the group who answered positively to the symptom of "*Persistent* flexural rash in the past 12 months?", there was a bigger proportion of cases (range 0.0% to 66.7% between study centres) that were not confirmed as flexural eczema on physical examination.

Likely contributory factors to these discrepancies include the following: i) Language and cultural differences without the aid of a video component could lead to misinterpretation of the questions; ii) The skin examinations were done by field workers and not dermatologists nor paediatricians; darker skin colours may lead to the condition being missed by a less experienced examiner; iii) Other pruritic skin conditions such as scabies may be reported as being eczema; and lastly, iv) Although the areas of buttocks and ears were part of the flexural areas in the written questionnaire, they were not included in the physical examination component. The latter omission was due to the fact that the physical

examination was based on the U.K. diagnostic criteria for atopic eczema which was only finalised after the ISAAC symptom-based questionnaire was drawn up.

In this regard, Czarnobilska et al. (2010) found that the ISAAC questionnaire was not specific enough to distinguish between atopic eczema, allergic contact dermatitis and other eczematous conditions. However, these findings were limited by the small sample size (n=143) as well as the recall bias of the respondents.

The United Kingdom Working Party (UKWP) criteria (also known as the UK diagnostic criteria) is another diagnostic tool that consists of a combination of standardized questions (used as part of the eczema core written questions of ISAAC) and a set of reference photographs. The original criteria consist of one mandatory and five major criteria; a diagnosis of atopic eczema is made with the fulfilment of a positive itch plus three criteria (Brenninkmeijer 2008).

Variable results between the UKWP criteria and ISAAC surveys for eczema have been summarised by Strina et al. (2010) and Brenninkmeijer et al. (2008) as being due to: the intermittent nature of the condition; the mild forms of eczema prevalent in the community that differ from those that present to health care facilities; recall bias among the parents and children and a denial of itching history by the parents; differences in study characteristics as well as different reference standards; different periods of prevalence to establish the diagnosis of eczema, and areas with a higher prevalence of scabies and other skin conditions than that of eczema.

The findings of the study showed that the prevalence estimates using the ISAAC questionnaire (11.3%) were almost twice the estimates of the UKWP protocol (5.9%).

A local Cape Town study of the point prevalence of atopic eczema using a modified version of the UKWP diagnostic criteria as well as a clinical assessment by a dermatologist also yielded variable results (Chalmers 2005). The point prevalence of atopic eczema following

clinical examination was 1.0% while the one-year prevalence according to the UK modified criteria was 1.8%.

However, the authors also noted that apart from one sign (presence of visible flexural eczema according to UKWP photograph), the use of the UKWP criteria as a diagnostic tool for atopic eczema was difficult to implement in a Xhosa-speaking population. Cultural understanding and translation issues were the main factors that were identified. Still, the sensitivity and specificity of the U.K. criteria compared to clinical diagnosis in this setting were relatively good at 43.7% and 97.9% respectively. The positive and negative predictive values were 18.4% and 99.4%.

The finding by Chalmers et al. (2005) that the UKWP photograph of flexural eczema was consistent with the clinical diagnosis, was confirmed by Haileamlak et al. (2005) who found in a cross-sectional survey in Ethiopia that the sign of visible flexural dermatitis examined for by a physician had higher positive and negative predictive values (57% and 91% respectively) than the ISAAC questionnaire (48.8% and 90.5%) and the UK criteria (55.5% and 90.1%). The authors admit that a limitation was their inability to examine the children within one week of the completion of the questionnaire which is the recommended time interval for assessing the symptom-based questionnaires against a point-prevalence based on a single physical examination. Extending this time interval by as much as two months meant that the physical signs of eczema may have either relapsed or now appeared.

1.2 Rhinitis symptoms

In 2009, the ISAAC questionnaire for allergic rhinitis and the Score for Allergic Rhinitis (SFAR), a questionnaire that assigns a quantitative score for allergic rhinitis in the absence of a medical visit (Piau 2009), were validated against the diagnosis made by a physician. The study was conducted on 597 adults and children in six countries: Morocco (Casablanca), Tunisia (Tunis) and Syria (Damascus), Ivory Coast (Abidjan), Congo (Brazzaville) and Guinea (Conakry). The findings are below in Table 1.2.

Apart from Guinea which had not significant findings, the SFAR had a much higher sensitivity than ISAAC across the board. The specificity of ISAAC was higher in 4 out of the 6 countries with no significant differences in 3 instances. However, the study had several limitations; the most important being that respondents were recruited from hospital clinics and may not be representative of the general population that ISAAC was intended for. Also, the mean age was 29.8 years (range 10.3 to 36.1) amongst the six countries; affecting the external generalizability of the findings, specifically to children and young adolescents.

In general, the ISAAC questionnaire appears to have a lack of specificity for its assessment of both symptoms. This is greater for the eczema component. However, this is offset by its sensitivity that appears appropriate for use at a population level.

Table 1 : Sensitivity and specificity of ISAAC and Score for Allergic Rhinitis (SFAR) tools compared to diagnosis of physician of rhinitis during no pollen season (Piau 2009)

	Sensitivity			Specificity		
	ISAAC (versus physician)	SFAR (versus physician)	Difference (Significance)	ISAAC (versus physician)	SFAR (versus physician)	Difference (Significance)
Congo	0.73	0.94	–0.21 (0.01)	0.98	0.84	0.14 (NS)
Guinea	0.79	0.6	0.19 (NS)	0.48	0.78	–0.30 (NS)
Ivory Coast	0.40	0.97	–0.57 (<0.0001)	1	0.7	0.30 (0.001)
Morocco	0.60	0.93	–0.33 (<0.0001)	0.84	0.56	0.28 (NS)
Syria	0.47	0.97	–0.50 (<0.0001)	0.84	0.64	0.20 (NS)
Tunisia	0.54	0.72	–0.18 (NS)	0.82	0.88	–0.06 (NS)

(NS-Not significant)

2. To review the most pertinent sociodemographic, dietary and environmental risk factors associated with allergic rhinitis and atopic eczema.

In general, the studies to measure and describe the determinants of allergic rhinitis and atopic eczema in children have been numerous, diverse and to a large extent contradictory in their findings (Torres Borrego 2008).

2.1 Diet

Dietary factors are an important consideration in the epidemiology of disease, especially non-communicable diseases. The antioxidant properties of foodstuffs (Ellwood 2001), trans-fatty acids (Weiland 1999, Asher 2010) and lineoleic acids in polyunsaturated fats have been the areas of focus for allergic diseases, in particular asthma and rhinitis.

In 2001, Ellwood et al. (2001) found in an ecological analysis significant (unadjusted for GNP though) protective associations between the outcomes of both allergic rhinoconjunctivitis and atopic eczema and i) calories from cereals and rice and ii) protein from cereals and nuts. There was also a protective association between vegetables and the symptoms of atopic eczema. This was particularly evident in the 13 to 14 year old age group. When adjusted for GNP, the protective associations for these and other categories such as seafood, all fish and olive oil, persisted although the significance waned.

In contrast, findings from the cohort of the Osaka Maternal and Child Health Study (Miyake 2007) showed no association of consumption of meat, eggs, and dairy products with the study definition of allergic rhinitis (either had received treatment with medications at some time in the previous 12 months or had another condition known as Japanese cedar pollinosis). A weak but significant protective and independent association was found between specific types of fatty acids (eicosapentaenoic and docosahexaenoic acids) and allergic rhinitis. Contrary to the ecological study of Ellwood et al., fish intake was not a significant protective factor for the outcome of allergic rhinitis.

In the analysis of asthma in the current ISAAC study, Mahlati (2007) found that maize consumption was consistently negatively associated with current wheeze. The fortification of maize-meal and other food products with micronutrients that have antioxidant properties and that may lessen the inflammatory response, may explain the negative associations with rhinitis and eczema. In contrast, eating pasta once or twice a week (compared to never eating pasta) increased the odds of current wheeze.

The consumption of fast food in relation to allergic disorders and atopy is an interesting potential risk factor. In New Zealand, Wickens et al. (2005) found that even "less than once a week" hamburger (defined as a beef mince patty in a bread roll) consumption was an independent predictor of current wheeze (adjusted OR 1.81, 95% CI 1.10–2.98) and having a history of wheeze (adjusted OR 1.65, 95% CI 1.07–2.52). Takeaway consumption (did not show an effect on any of the three outcomes. The intake of fast food may be a marker of high SES but other factors such as the salt content need to be considered in the interpretation of the associations with allergic disorders.

In conclusion, current epidemiological studies are inconclusive on the role of different food types and their association with allergic rhinitis and eczema. Starch and cereal foodstuffs as well as seafood are the dietary factors that may have a protective influence on the two allergic conditions. Fast food consumption may be a risk factor.

2.2 Body Mass Index (BMI)

The relationship between obesity and allergic disorders is topical but not straightforward.

Leptin, an adipocyte-derived protein hormone, is thought not only to be involved in body weight regulation but also in the immune response (Quek 2010). Previous studies have suggested that children who were overweight as measured by higher leptin levels were at an increased risk of asthma (Guler 2004).

Quek et al. (2010) found that the higher BMI and serum leptin levels were associated with the diagnosis of asthma but not in those children with only allergic rhinitis. A cross-sectional

study in Japan (Yoshida 2010) were consistent with the findings of Mahlati (2007) - their results suggested a positive association between being overweight (definition for exposure was above 90th percentile of BMI for age and gender) and the prevalence of current wheeze in adolescents. The association with the symptoms of current rhinoconjunctivitis was not statistically significant. However, the lack of temporality associated with a cross-sectional study design poses a challenge in the interpretation of findings.

Other studies such as Kajbaf et al. (2011) and Vlaski et al. (2006) were unable to find a significant association between being overweight and symptoms of wheezing, rhinitis or eczema. Both studies instead found significant associations with “dry night cough”, a non-specific sign of asthma.

Other conditions such as gastro-oesophageal reflux and obstructive sleep apnoea, that are associated with being overweight, may mimic respiratory symptoms; hence the association with this non-specific sign but not others of asthma. In conclusion, the evidence presented for obesity or overweight-for-age as a strong risk factor for any of the three allergic conditions is not convincing.

2.3 Home environment

The degree of protection or risk of an urban or rural environment associated with allergic conditions, whether as part of upbringing or current residence, differs between countries. This may be due to the definitions applied in different studies as well as the influence of other exposures such as population genetics and environmental factors (Nicolaou et al. 2005).

The role of the home environment in the development and severity of allergic conditions is well known. In a diverse and inequitable country such as South Africa, not all people live in housing that is protective against the weather elements.

Ibargoyen-Roteta et al. (2007) found that exposure to moisture and mould on the house walls in the first year of life was a significant risk factor for current allergic rhinoconjunctivitis

symptoms, but not those of atopic eczema. With multivariate analysis, the effect of moisture on walls was attenuated but still significant.

Mahlati (2007) found that living in a shack (compared to a house) and overcrowding were inversely associated with the outcome of current wheeze and an asthma diagnosis on the written questionnaire. However, both variables were attenuated in the multivariate analysis. A 2005 Ethiopia study (Haileamlak 2005) found that the risk of atopic eczema was unrelated to family size and overcrowding at home but was inversely related to access to piped drinking water. The latter also confirmed the findings of increased odds of the condition with better parental education (secondary schooling adjusted for age, sex and site OR1.65, 95% CI 1.07-2.55). Drinking from the river which is associated with a lower SES is thought to have a protective effect through increased exposure to enteric infections.

The benefits for allergy of a more rural upbringing were also demonstrated in a Swedish cross-sectional study (Eriksson 2010) of 16 to 75 year old respondents. Living on a farm for the first five years of life was associated with a lower prevalence estimate of allergic rhinitis (20.1%) than those who were not raised in a farming environment (28.0%). This prevalence increased with increasing degrees of urbanization (from rural area to small town to mid-sized town to metropole). Endotoxin, part of the cell wall of Gram-negative bacteria, is thought to be the main factor responsible for the protective effect of the farming environment. Exposure to endotoxin and similar components are thought to enhance the non-allergenic T-helper 1 response to a greater extent than T-helper 2. The study does suffer from traditional cross-sectional design flaws and the authors admit that they did not measure exposures such as parental smoking habits, history of childhood infections and number of siblings. Despite this, the protective effect of childhood farm living in relation to allergic rhinitis and in particular on young adults (OR 0.78, 95% CI 0.64–0.95) was confirmed.

2.4 Gender

Osman et al. (2007) found that for both asthma and rhinitis, the initial male predominance observed in childhood reversed at adolescence. The female predominance for eczema was noted to be earlier at 5 years of age but peaked considerably around adolescence. Despite these gender-specific presentations of allergic outcomes, the variable of gender on allergic disease, especially with respect to the ISAAC data, is not thoroughly explored in many studies.

Possible explanations for an excess of female self-reporting of general physical and psychological symptoms at adolescence (Sweeting 2003) include the following influences: normal physical and maturational cycles which may be more positive for boys than females; societal influences on gender roles (Osman 2007); different coping mechanisms and different perceptions of symptoms (Hetland 2002).

2.5 Smoking

Study of the effects of passive smoking on allergic disorders in older children and adolescents has also yielded conflicting results (Torres-Borrego 2008). Some studies such as Annesi-Maesano et al. (2004) have reported significant positive associations with all three allergic conditions, others show positive findings for respondent smoking only (Burr 1999) and while studies of Raherison et al. (2006), Strachan et al. (1998) and Vlaski et al. (2010) show no associations at all.

Using the self-reported data from ISAAC Phase Three of the Skopje centre, Republic of Macedonia, Vlaski et al. (2010) found that apart from the significant finding of maternal smoking and current night dry cough adjusted for confounders such as gender, educational level etc. (OR 1.03, 95% CI 1.03-1.54) no significant associations existed between smoking variables and eczema or rhinitis. The authors cite information bias as a possible limitation in their findings as the adolescents may not have fully understood the questions. The environment of the country is also such that children are more likely to be outdoors and therefore not completely exposed to the smoking habits of either parent. However, the

absence of any associations may be an accurate reflection as, despite reported high tobacco smoking estimates in the country, the prevalence of both symptoms is very low (prevalence of rhinoconjunctivitis symptoms 5.8% and current eczema symptoms 2.7%).

Although they do not report the actual prevalences of rhinitis and eczema, Raherison et al. (2006) state that they found no association between exposure to environmental tobacco smoke (ETS; represented by parental smoking habits in the study) and recent allergic rhinitis in children. Contrary to expectation, they also report finding a negative association between current ETS exposure and lifetime hay fever (defined as a history of hay fever at least once in life) and eczema.

The effect of smoking thus appears to depend on whether it is active (the respondent) or passive and the exposure patterns. Parents may temporarily cease smoking while their child is ill or smoke but not in the immediate vicinity of the child. This may result in misclassification of exposure as there may be overestimation of the children's exposure to smoke.

2.6 Truck traffic frequency

Truck traffic is another interesting environmental risk factor as it may affect these allergic conditions through several mechanisms. These could be either inflammatory or adjuvant pathways that may cause or aggravate symptoms by allergic sensitisation. Alternatively, truck traffic may be a marker of deprivation and be a contributory cause of stress which may aggravate an allergic condition such as eczema.

Brunekeef et al. (2009) conducted an ecological analysis of 238 centres in 98 countries (513, 087 children) for which data on self-reported truck traffic exposure was reported. In Africa, 31.6% of 13 to 14 year old children reported "high" exposure (almost the whole day) compared to only 7.9% reported in Western Europe. After adjustment for a variety of confounders, there were still significant findings between high versus never truck traffic and

rhinoconjunctivitis (OR 1.39, 95% CI 1.27-1.52); as well as eczema (OR 1.54, 95% CI 1.37-1.73).

In contrast, although only followed to 3 years of age, the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS), a prospective birth cohort study of children born to atopic parents, found no association between exposure to Elemental Carbon Attributable to Traffic (ECAT) in infancy and allergic rhinitis or atopy (Codispoti 2010).

2.7 Acetaminophen (paracetamol)

Acetaminophen is yet another risk factor that has been explored in ISAAC. Several mechanisms of action that paracetamol exerts on allergic conditions have been postulated (Farquhar 2009). These include a depletion of glutathione-dependent enzymes which may impair antioxidant defences but also lead to a greater T-helper type 2 cytokine production, predisposing to an allergic response. An alternative mechanism is via suppression of the natural immune response (predominant T-helper type 1 response) when pyrexia is dampened. Both mechanisms will either lead to an exacerbation of allergic conditions such as rhinitis and eczema or prolong the recovery from the condition. Twenty years ago, Graham et al. (1990) demonstrated in a randomized controlled trial that both aspirin and acetaminophen were significantly associated with a suppressed antibody response. Prymula et al. (2009) confirmed the reduced antibody response when acetaminophen was prophylactically administered at the time of vaccination.

Beasley et al. (2010) found that there was an exposure-dependent increased risk of current symptoms of rhinoconjunctivitis and eczema when paracetamol was used in adoescents. The population-attributable risk (PAR) for current symptoms of rhinoconjunctivitis and eczema associated with current paracetamol use was calculated as 36% and 40% respectively, assuming that the associations are causal. This association was independent of the presence of asthma although the authors recognised that the findings could be limited by confounding by indication (paracetamol used to treat symptoms of rhinitis) and by recall bias.

In 2000, Newson et al. showed in an ecological study that there was a positive significant association between high prevalences of allergic outcomes in English-speaking ISAAC countries and national paracetamol sales. However, after controlling for the effect of these countries, with the exception of atopic eczema in adolescents, these associations were attenuated and became non-significant.

More recently, the Cape Town Phase Three asthma analysis by Mahlati (2007) suggested that paracetamol used at least once a month had an association with the reporting of current wheeze (multivariate analysis OR 1.2, 95% CI 1.0- 1.4). Elsewhere, Cohet et al. (2004) also found that recent use of paracetamol at least once per month was associated with rhinoconjunctivitis but not eczema amongst 6 to 7 year old children in New Zealand.

Asher et al. (2010) also demonstrated on an ecological level a small but positive association of rhinitis and eczema with paracetamol use.

In conclusion, there is biological plausibility for the positive association of paracetamol use with allergic rhinitis and atopic eczema. The conflicting results of current studies suggest the need for a stronger study design and methods that reduce the confounding and other biases. This evidence may have been provided by Lowe et al. (2010) who found in a prospective cohort study that the association between paracetamol use and an increased risk of asthma disappeared after i) adjustment for history of early infections and ii) restriction to paracetamol use for non-respiratory tract illness. This also applied to the outcomes of rhinitis and eczema.

2.8 Tuberculosis

In 1997, Shirakawa and Enomoto found an inverse association between the prevalence of allergic disease and delayed hypersensitivity to Bacille–Calmette–Guerin (BCG) vaccination in children. It was in keeping with the thinking that a stimulated T-helper type 1 response would curb the atopic pathway (Steenhuis 2007). Steenhuis et al. (2007) were unable to demonstrate a 50% reduction in the prevalence of allergic disease in high-risk 18-month old

infants after the 6-week administration of BCG compared to the placebo group. However, the BCG group did demonstrate a trend towards less eczema (RR 0.72, 95% CI 0.5–1.0) and significantly less use of medication for eczema (RR 0.58, 95% CI 0.3–1.0) than the placebo group at the age of 18 months.

Miyake et al. (2007) found that in 6 to 7 year old children, positive tuberculin reactivity was protective for atopic eczema symptoms but not allergic rhinoconjunctivitis symptoms.

In contrast, Soysal et al. (2008) conducted a study amongst 347 household contacts (mean age 8 years, SD 4 years) of adult patients with sputum smear-positive pulmonary TB. They reported no significant difference between the frequencies of “ever wheeze”, “ever asthma”, allergic rhinitis symptoms and atopic dermatitis symptoms in BCG scar-negative and –positive contacts. This suggests M. tuberculosis infection may not have the protective effects on the development of atopy as speculated in other studies.

The strains of BCG (Miyake 2007), the timing of the mycobacterial inhibition of atopy in life (Soysal 2008) as well as the influence of environmental factors on the strength and different mechanisms of immune response are factors to consider in the role that TB plays in allergic disease.

3. To review the influence of upward social mobility on the symptoms of allergic rhinitis and atopic eczema.

Maternal education is often used as a proxy measure of SES. A tertiary education for the maternal caregiver (versus not a tertiary level) was a risk factor for the outcomes of current wheeze and an asthma diagnosis on the written questionnaire. These associations suggest that a higher SES provides individuals with not only the means to access health care and be diagnosed earlier but that they are more likely to report symptoms that someone with lower SES may not perceive as a priority. The protective effect of a low SES may be due to the development of atopy by an increased exposure to microbial agents in poorer living conditions as per the hygiene hypothesis (Dom 2009).

A Swedish cohort study (Braback 2005) found that although low SES was a risk factor for asthma and protective for allergic rhinitis, steep increases in both conditions across three succeeding birth cohorts were observed amongst this group. Compared to the high SES group, the inverse association between low SES and rhinitis was becoming weaker: 1952-1961 cohort, OR 0.79 (0.77–0.81); 1962-1971 cohort, OR 0.83 (0.82–0.86) and 1972-1977 cohort, OR 0.92 (0.90–0.94). The authors felt that this demonstrated a more improved social class effect as there had been a dramatic improvement in the standard of living in Sweden; promoting allergic disease according to the hygiene hypothesis.

Thus far, two studies of the Phase One Cape Town centre ISAAC data have found associations between the students from low SES areas attending schools located in higher SES areas and the outcomes of recent wheeze, rhinitis and eczema (Poyser 2002; Mercer 2004). In Poyser et al. (2002), although the written questionnaire showed that the highest prevalences of asthma and recent wheeze were found amongst the higher SES students attending high SES schools, in the video questionnaire the prevalence of asthma symptoms in the last 12 months was considerably higher amongst the low SES students attending high SES schools; i.e. the “commuting” adolescents.

Other ISAAC studies that have measured social mobility in terms of residence and schools and their associations with rhinitis and eczema outcomes were not found.

III. LITERATURE REVIEW: CONCLUSION

In conclusion, the literature reviewed for the validation of the ISAAC instruments demonstrates that, despite not having an adequate specificity, the symptom-based questionnaire of ISAAC for both eczema and rhinitis is sensitive for use at a population level and has brought an element of standardisation to the assessment of allergic conditions in different countries. In the case of atopic eczema, the addition of photographic materials such as in the UKWP would have required extra resources (e.g. staff training) and may not have increased the specificity of the questionnaire substantially. For rhinitis, deficiencies such as translation and cultural interpretation could have been reduced with a video component as was done for the symptoms of asthma.

In general, the main dietary exposures of starch, cereal and seafood appear to be protective while fast food consumption a risk for allergic symptoms. Factors such as the cultural understanding of the food stuffs in the questionnaire, the portions that are consumed to constitute consumption to be a risk or protective and the role of diet amidst other influences (sociodemographic and environmental) are still unanswered.

The association between overweight-for-age and allergic disease may be confounded by other medical conditions that mimic the symptoms of allergic disease.

Environmental exposures such as truck traffic frequency, smoking and the use of paracetamol have biologically plausible mechanisms for positive associations with the outcomes.

An inverse association between socioeconomic status and allergic disease may exist. Previous ISAAC Phase One Cape Town studies of the “upwardly mobile” group have shown evidence of this association. Although the numbers of this group of students was small, it does warrant an assessment of Phase Three data as there appears to be a paucity of research into this area.

ISAAC Phase Three data has not yet been analysed in terms of rhinitis and eczema outcome measures and further analysis of this data may yield findings that could assist in frameworks of allergic disease intervention for prevention or stabilisation of increasing trends.

Part C: Manuscript

Title: **Sociodemographic, dietary and environmental determinants of allergic rhinitis and atopic eczema symptoms among South African adolescents: findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three Study, Cape Town, South Africa**

Key words: **ISAAC; allergic rhinitis; eczema; Cape Town**

I. INTRODUCTION

Concerns about increasing allergic disease in both developed and developing countries have stimulated extensive research in the past two decades. The three phases of the International Study of Asthma and Allergies in Childhood (ISAAC) in study centres throughout the world have provided a standardized methodology and the means to conduct baseline prevalence studies of rhinitis, eczema and asthma in school goers (Asher 1995 and 1998) as well as to measure the determinants of variation between study centres (Weiland 2004; Ellwood 2005).

The Cape Town centre participated in Phases One and Three of ISAAC. Using this data, a significant increase in the lifetime and 12-month prevalence of both allergic rhinitis and eczema symptoms has been shown (Zar 2007).

In general, there have been inconclusive findings for many of the possible determinants of the outcomes of rhinitis and eczema across study centres (Ellwood 2001; Huang 2001; Chatzi 2009; Asher 2010). Analysis of the Cape Town dataset for the predictors of risk of rhinitis and eczema has to date not been conducted.

The research aim of this study was therefore to investigate the association of allergic rhinitis and atopic eczema symptoms with sociodemographic, dietary and environmental risk factors in the 13 to 14 year old group of adolescents who were studied in the Cape Town, South Africa centre of the ISAAC Phase Three study.

Objectives of the study were to:

a. To measure and analyse risk factors associated with reported allergic rhinitis and atopic eczema symptoms.
b. To identify risk factors common to both conditions, as well as to current wheeze symptoms that was analysed by another researcher in 2007 using the same dataset.
c. To measure and analyse risk factors amongst those adolescents with both allergic rhinitis and atopic eczema (comorbid) symptoms.

d. To measure the influence of upward social mobility on rhinitis and eczema symptoms.

II. METHODS

A cross-sectional study design using standardized ISAAC written and video (for asthma) questionnaires was performed in 2002. The study population in the ISAAC study included adolescents who attended randomly selected schools from 3 racially constituted strata in Cape Town. Each school was visited twice to ensure that all eligible adolescents that may have been skipped as a result of absenteeism were included.

Ethics approval for the 2002 ISAAC study was granted by the Research Ethics Committee of the University of Cape Town. All relevant stakeholders were also consulted and approached for permission.

Data analysis was done using Stata version 11.1 software (Stata Corporation, June 2010). Logistic regression with stepwise model-building was done until the best model, including sociodemographic, dietary and environmental variables for each outcome of allergic rhinitis and eczema, was selected.

A marker of upward mobility was analysed using “commuting status” of the adolescents. The study schools were classified into low SES or high SES based on the name and location of the school, as judged by the researcher. Thereafter, the residential suburb as provided by the participant was classified into “low” or “high” SES. Those adolescents residing in the lower SES areas but attending schools in affluent areas were classified as “commuters”. The comparison groups were adolescents residing in and attending schools located in the same area; that is, whether low SES or higher SES areas.

III. RESULTS

3.1 Background characteristics of respondents

The analysis was conducted on 5, 037 respondents from 54 schools in the Cape Town Metropole district. A total of 59.5% (2, 995) of the respondents were female and English was the predominant language of instruction at the sampled schools (40.9%). Only 18.5% (934) of the respondents were not born in Cape Town. The most prevalent maternal educational level that was reached was high school (58.8%) and 11.4% of respondents lived in an informal dwelling (shack). All the prevalence estimates are available in the Online Repository: Table i-iii (Appendix II).

3.2 Prevalence of rhinitis, eczema and comorbid outcomes

Totals of 20.7% (1, 043) and 13.3% (670) of the respondents reported experiencing symptoms of allergic rhinitis and atopic eczema respectively. 212 (4.2%) of respondents reported that rhinitis symptoms had a significant impact on their daily activities.

Table 2: **Core written questions and Rhinitis symptoms**

Symptom	n	N	Percentage (%)
Ever rhinitis	2, 466	5, 037	49.0
Rhinitis in past 12 months	1, 939		38.5
Rhinitis and conjunctivitis in past 12 months	**1, 043**		**20.7**
Hayfever ever	2, 088		41.5
Impact on daily activities:			
Not at all	643	5, 037	12.8
A little	1, 321		26.2
A moderate amount	376		7.5
A lot	212		4.2

Table 3 Core written questions and Eczema symptoms

Symptom	n	N	Percentage (%)
Ever itchy rash	1, 318	5, 037	26.2
Itchy rash in past 12 months	975		19.4
Itchy rash in flexural areas on body	**670**		**13.3**
Eczema ever	839		16.7
Sleep disturbed in past 12 months:			
Never in the past 12 months	946	5, 037	18.8
Less than one night per week	499		9.9
One or more nights per week	292		5.8

In all, 436 (8.7%) of 5, 037 respondents reported that they had experienced symptoms of both rhinitis and eczema in the past 12 months (not shown). Females comprised 74.1% (323) of this group. Fewer respondents reported that they had experienced both allergic rhinitis and atopic eczema symptoms: 244 (4.8%). No other striking findings were noted from this comorbid group.

3.3 Comparison of bivariate associations of allergic rhinitis, eczema and wheeze symptoms with selected sociodemographic, dietary and environmental exposures

Tables 4, 5 and 6 present the bivariate associations of selected sociodemographic, dietary and environmental factors associated with the outcomes measures. The findings of Mahlati (2007) for the outcome of current wheeze (wheeze in the past 12 months) on the *written* (not video) questionnaire were reported alongside those of allergic rhinitis and atopic eczema for selected variables. The full outputs for allergic rhinitis and eczema are available in Tables iv

and v in the Online Repository (Appendix II). The increased specificity of the outcomes (see "Definitions") has meant that statistical power is reduced.

In this analysis (Table 4), Xhosa compared to the reference category of Afrikaans was a stronger risk factor for eczema. English as the medium of instruction compared to Afrikaans at schools was a risk factor for all three outcomes.

Male gender was inversely associated with both allergic rhinitis and atopic eczema; wheeze was not associated with gender (Mahlati 2007). Tertiary maternal education was suggestive as a risk factor for allergic rhinitis and wheeze outcomes but protective for atopic eczema. People employed in the household appear to be a risk factor for both allergic rhinitis and wheeze; while unemployed household members is suggestive to be a risk factor for atopic eczema.

Tables 5 and 6 below present selected bivariate analyses of environmental and dietary variables.

Despite a lack of statistical power, the use of wood (including open fires) for cooking and heating was a predictor of the odds of all three outcomes. The use of wood (including open fires) for cooking was statistically significant when the outcome was all-cause rhinitis (OR 1.89 95% CI 1.20-2.97). The use of paraffin for cooking and heating– suggestive of low SES – was a statistically significant risk factor for rhinitis and eczema.

In general, measures such as access to electricity and taps were suggestive of risk factors for allergic rhinitis and wheeze but protective for atopic eczema.

A shack dwelling (reference category: house) was positively associated with atopic eczema but protective for wheeze.

The positive effect of Paracetamol (use at least once a month) as a risk factor was consistently seen for all three outcome measures. Although not statistically significant for the

allergic rhinitis outcome, maternal cigarette smoking and smoking by the respondent appear to be risk factors for the outcomes of allergic rhinitis and wheeze.

Having received treatment for TB or having a household member who has had TB were significant predictors of odds for atopic eczema.

Significant effects of some of the dietary factors were observed with an intake of three or more times a week (versus less often or never). However, apart from pulses, pasta, cereals and maize which showed a similar trend for at least two of the outcomes, the rest of the findings were inconsistent and not significant across the three outcomes.

Table 4: Bivariate associations of allergic rhinitis, atopic eczema and wheeze symptoms with selected sociodemographic exposures

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
Language of instruction									
Afrikaans	258	1, 289	1.00	99	1, 289	1.00	204	1, 289	1.00
Xhosa	297	1, 689	1.40 (1.15-1.71)	352	1, 689	4.22 (3.28-5.42)	224	1, 689	0.8 (0.6-1.0)
English	488	2, 059	1.43 (1.20-1.72)	219	2, 059	1.89 (1.46-2.45)	597	2, 059	2.1 (1.8-2.6)
Sex									
Female	701	2, 995	1.00	455	2, 995	1.00	-	2, 995	1.00
Male	339	2, 026	0.61 (0.53-0.71)	211	2, 026	0.60 (0.50-0.73)	-	2, 026	-
What level of education has your mother reached or completed?									
Primary school	-	4, 115	1.00	-	4, 115	1.00	-	4, 115	1.00
	211	922	1.04 (0.87-1.27)	129	922	0.91 (0.73-1.13)	192	922	1.03 (0.86-1.24)
Secondary school	-	2, 077	1.00	-	2, 077	1.00	-	2, 077	1.00
	601	2, 960	0.94 (0.81-1.09)	383	2, 960	0.91 (0.76-1.09)	558	2, 960	0.80 (0.69-0.92)
Tertiary education	-	3, 951	1.00	-	3, 951	1.00	-	3, 951	1.00
	240	1, 086	1.13 (0.95-1.34)	128	1, 086	0.98 (0.78-1.22)	297	1, 086	1.66 (1.42-1.95)
Do you have a TV in your house?									
Yes	951	4, 504	1.27 (0.93-1.74)	568	4, 504	0.60 (0.44-0.80)	932	4, 504	1.30 (0.96-1.76)

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
No	57	346	1.00	78	346	1.00	58	346	1.00
How many people in your household are working?									
0	52	289	1.00	44	289	1.00	46	289	1.00
1	313	1, 549	1.16 (0.82-1.64)	233	1, 549	1.01 (0.74-1.59)	282	1, 549	1.17 (0.83-1.69)
2	364	1, 707	1.20 (0.85-1.69)	207	1, 707	0.87 (0.59-1.28)	388	1, 707	1.55 (1.10-2.22)
3	128	598	1.18 (0.81-1.74)	88	598	1.06 (0.69-1.62)	129	598	1.45 (0.99-2.15)
≥4	77	352	1.14 (0.75-1.73)	39	352	0.66 (0.40-1.08)	80	352	1.55 (1.02-2.37)
How many people in your household are not working?									
0	354	1, 652	1.00	195	1, 652	1.00	408	1, 652	1.00
1	315	1, 507	0.90 (0.75-1.09)	206	1, 507	1.11 (0.92-1.34)	282	1, 507	0.70 (0.58-0.83)
2	137	724	0.87 (0.69-1.10)	129	724	1.51 (1.21-1.89)	114	724	0.56 (0.44-0.71)
3	56	251	1.06 (0.75-1.50)	43	251	1.36 (0.97-1.90)	42	251	0.61 (0.42-0.87)
≥4	32	150	1.00 (0.64-1.56)	24	150	1.34 (0.88-2.04)	30	150	0.76 (0.48-1.16)

Table 5: Bivariate associations of allergic rhinitis, atopic eczema and wheeze symptoms with selected environmental exposures

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
In your house, what fuel is usually used for cooking?									
Electricity	-	599	1.00	-	599	1.00	-	599	1.00
	919	4, 436	0.90 (0.72-1.13)	585	4, 436	0.97 (0.74-1.26)	911	4, 432	1.10 (0.88-1.37)
Gas	-	4, 531	1.00	-	4, 531	1.00	-	4, 531	1.00
	129	503	1.51 (1.19-1.91)	80	503	1.27 (0.96-1.67)	96	502	0.91 (0.71-1.16)
Paraffin	-	4, 145	1.00	-	4, 145	1.00	-	4, 145	1.00
	167	892	1.30 (1.06-1.60)	196	892	2.35 (1.91-2.90)	136	892	0.65 (0.53-0.80)
Wood	-	4, 954	1.00	-	4, 954	1.00	-	4, 954	1.00
	23	83	1.23 (0.74-2.06)	12	83	1.21 (0.61-2.39)	23	83	1.51 (0.88-2.49)
In your house, what fuel is usually used for heating?									
Electricity	-	1, 496	1.00	-	1, 496	1.00	-	1, 496	1.00
	770	3, 540	1.01 (0.86-1.20)	419	3, 540	0.64 (0.53-0.78)	753	3, 540	1.21 (1.03-1.42)
Gas	-	4, 806	1.00	-	4, 806	1.00	-	4, 806	1.00
	64	231	1.32 (0.96-1.81)	27	231	0.78 (0.54-1.15)	61	231	1.43 (1.04-1.94)
Paraffin	-	3, 856	1.00	-	3, 856	1.00	-	3, 856	1.00
	231	1, 177	1.35 (1.21-1.61)	241	1, 177	2.23 (1.84-2.71)	176	1, 177	0.62 (0.52-0.74)

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
Wood	-	4, 733	1.00	-	4, 733	1.00	-	4, 733	1.00
	66	303	1.07 (0.79-1.44)	39	303	1.07 (0.73-1.56)	81	303	1.46 (1.11-1.91)
Is your house damp or wet inside?									
Yes	118	507	1.32 (1.03-1.67)	106	507	1.78 (1.38-2.31)	93	507	0.85 (0.66-1.08)
No	885	4, 305	1.00	536	4, 305	1.00	896	4, 305	1.00
Do you have taps for running water in your house?									
Yes	821	3, 861	1.16 (0.95-1.39)	497	3, 861	0.95 (0.77-1.18)	836	3, 861	1.52 (1.25-1.86)
No	324	933	1.00	205	933	1.00	143	933	1.00
Do you have electricity in your house?									
Yes	981	4, 666	1.61 (1.02-2.53)	617	4, 666	0.97 (0.63-1.50)	964	4, 666	1.55 (1.01-2.46)
No	51	181	1.00	34	181	1.00	26	181	1.00
In the past 12 months, how often, on average, have you taken Panado?									
Never	221	1, 333	1.00	148	1, 333	1.00	214	1, 333	1.00
At least once/year	337	1, 764	1.14 (0.93-1.38)	232	1, 764	1.22 (0.97-1.55)	351	1, 764	1.29 (1.07-1.57)
At least once/month	452	1, 741	1.80 (1.48-2.18)	267	1, 741	1.43 (1.13-1.80)	434	1, 741	1.73 (1.44-2.09)
Does your mother (or female care giver) smoke cigarettes?									
Yes	328	1, 405	1.07 (0.92-1.25)	145	1, 405	0.53 (0.43-0.65)	339	1, 405	1.34 (1.15-1.57)
No	672	3, 419	1.00	509	3, 419	1.00	652	3, 419	1.00

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
Do you smoke cigarettes?									
Yes	121	433	1.22 (0.96-1.54)	54	433	0.70 (0.51-0.96)	126	433	1.67 (1.33-2.10)
No	888	4, 417	1.00	594	4, 417	1.00	868	4, 417	1.00
Has anyone in your household ever had TB?									
Yes	165	691	1.40 (1.13-1.72)	149	691	1.95 (1.55-2.45)	133	691	0.91 (0.74-1.12)
No	839	4, 133	1.00	496	4, 133	1.00	854	4, 133	1.00
Have you ever been treated for TB?									
Yes	70	325	1.03 (0.77-1.38)	57	325	1.41 (1.01-1.97)	71	325	1.11 (0.83-1.46)
No	920	4, 447	1.00	579	4, 447	1.00	893	4, 447	1.00
What type of home do you have?									
House	821	3, 936	1.00	470	3, 936	1.00	836	3, 936	1.00
Flat	64	263	1.31 (0.95-1.80)	35	263	1.11 (0.75-1.66)	53	263	0.93 (0.67-1.28)
Shack	107	573	1.18 (0.92-1.52)	135	573	2.43 (1.90-3.11)	86	573	0.65 (0.50-0.83)
Other	12	60	0.74 (0.39-1.44)	7	60	0.90 (0.38-2.07)	12	60	0.92 (0.44-1.78)
How many people share your bedroom at night?									
0	258	1, 201	1.00	137	1, 201	1.00	300	1, 201	1.00
1	256	1, 285	0.86 (0.69-1.06)	168	1, 285	1.02 (0.78-1.32)	257	1, 285	0.75 (0.61-0.91)
2	232	1, 078	0.91 (0.73-1.13)	161	1, 078	1.05 (0.81-1.38)	207	1, 078	0.71 (0.58-0.87)
3	114	544	0.89 (0.68-1.16)	74	544	0.90 (0.65-1.25)	101	544	0.68 (0.52-0.88)

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
≥4	89	417	0.96 (0.72-1.29)	72	417	1.25 (0.88-1.75)	61	417	0.51 (0.37-0.70)

Table 6: Bivariate associations of allergic rhinitis, atopic eczema and wheeze symptoms with selected dietary exposures

	Allergic Rhinitis			Atopic Eczema			Wheeze (Mahlati 2007)		
Exposure	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**	**n**	**N**	**OR (95% CI)**
Pulses (peas, beans)									
Never or rarely	318	1, 561	1.00	173	1, 561	1.00	350	1, 561	1.00
Once or twice a week	462	2, 274	1.06 (0.89-1.25)	297	2, 274	1.32 (1.06-1.63)	467	2, 274	0.89 (0.76-1.04)
3 or more times a week	211	929	1.23 (1.00-1.53)	158	929	1.72 (1.34-2.22)	175	929	0.80 (0.65-0.98)
Pasta									
Never or rarely	257	1, 332	1.00	208	1, 332	1.00	247	1, 332	1.00
Once or twice a week	537	2, 434	1.04 (0.87-1.24)	283	2, 434	0.69 (0.56-0.86)	557	2, 434	1.30 (1.00-1.50)
3 or more times a week	181	827	0.98 (0.78-1.23)	120	827	0.72 (0.55-0.94)	167	827	1.10 (0.80-1.30)

Cereal (including bread)									
Never or rarely	83	459	1.00	53	459	1.00	89	459	1.00
Once or twice a week	168	842	1.13 (0.83-1.54)	119	842	1.44 (1.00-2.08)	184	842	1.16 (0.86-1.56)
3 or more times a week	756	3, 438	1.33 (1.23-1.74)	457	3, 438	1.46 (1.06-2.01)	715	3, 438	1.09 (0.85-1.41)
Maize									
Never or rarely	504	2, 224	1.00	237	2, 224	1.00	573	2, 224	1.00
Once or twice a week	297	1, 651	0.79 (0.67-0.94)	231	1, 651	1.35 (1.09-1.66)	265	1, 651	0.50 (0.40-0.60)
3 or more times a week	190	879	1.02 (0.83-1.26)	163	879	1.79 (1.41-2.27)	138	879	0.50 (0.40-0.60)

3.4 Comparison of multivariate associations of allergic rhinitis, eczema and wheeze symptoms

Table 7 presents the findings of multivariate analyses. The findings for outcome of wheeze were based on the *written* (not video) questionnaire of the study by Mahlati (2007).

Table 7: Summary of multivariate associations for the symptoms of allergic rhinitis, atopic eczema and wheeze

Risk factor	Allergic Rhinitis OR (95% CI)	Atopic Eczema OR (95% CI)	Wheeze (Mahlati 2007) OR (95% CI)
Sociodemographic factors			
Language of instruction at school: Afrikaans (reference category)	1.00	1.00	1.00
English	1.43 (1.18 – 1.72)	1.85 (1.41 – 2.41)	1.8 (1.5 – 2.1)
Xhosa	1.40 (1.13 – 1.73)	3.87 (2.97 – 5.05)	0.9 (0.7 – 1.1)
Male gender	0.66 (0.56 – 0.77)	0.62 (0.51 – 0.75)	-
Maternal primary school (versus higher)	1.12 (0.92 – 1.35)	0.96 (0.76 – 1.22)	-
TV in house (vs. no TV in house)	1.19 (0.92 – 1.55)	0.87 (0.66 – 1.14)	-
Dietary factors (unless otherwise stated, reference is no or occasional exposure)			
Maize three or more times a week	1.12 (0.91 – 1.37)	1.13 (0.90 – 1.43)	0.8 (0.6 – 1.0)
Cereal three or more times a week	1.28 (1.08 – 1.51)	1.31 (1.07 – 1.60)	-

Risk factor	Allergic Rhinitis OR (95% CI)	Atopic Eczema OR (95% CI)	Wheeze (Mahlati 2007) OR (95% CI)
Other environmental factors (unless otherwise stated, reference is no or occasional exposure)			
Paracetamol use at least once a month	1.58 (1.35 – 1.84)	1.26 (1.04 – 1.53)	1.4 (1.2 – 1.6)
House damp and wet inside (vs. not damp and wet)	1.28 (0.99 – 1.65)	1.39 (1.05 – 1.84)	-
Household member with TB ever (vs. no TB ever in household)	1.33 (1.07 – 1.66)	1.42 (1.12 – 1.82)	-
Respondent smoking	1.31 (1.03 – 1.67)	-	1.4 (1.1 – 1.8)
Wood or open fires as cooking fuel (vs. other fuel sources)	1.30 (0.77 – 2.21)	-	-

Some statistically significant associations that were observed in the bivariate analyses were attenuated; others became statistically significant for another outcome during the stepwise model-building.

Although both Xhosa and English had significant associations with both allergic rhinitis and atopic eczema, the former language of instruction was a stronger predictor for the outcome of eczema. Male gender was protective for both outcomes. Frequent paracetamol use (at least once a month) was a consistent finding for all allergic outcomes. Cereal consumption was a risk factor for rhinitis and eczema outcomes.

A household member with TB was a predictor for both allergic outcomes. Exposure to wood or open fires as cooking fuel was not statistically significant for allergic rhinitis but had been found to be when all-cause rhinitis was the outcome (OR 2.00; 95% CI1.26 – 3.18).

3.5 Multivariate associations of allergic rhinitis and atopic eczema (comorbid) symptoms

The Online Repository contains the bivariate analyses for those adolescents with both allergic rhinitis and atopic eczema outcomes (comorbid).

Table 8 showed that while Xhosa and English were significant risk factors. Consumption of cereal and maize appear to be positively associated – although not statistically significant - with comorbid symptoms. As expected, paracetamol use at least once a month was a predictor. A household member with TB was positively associated with greater odds of having both symptoms. In general, the associations were a combination of factors that emerged from the individual conditions.

Table 8: Multivariate analysis: association of sociodemographic, dietary and environmental factors with allergic rhinitis and atopic eczema (comorbid) symptoms

Risk factor	OR	95% CI
Sociodemographic factors		
Language of instruction at school:		
Afrikaans (reference category)	1.00	-
English	1.51	1.04-2.20
Xhosa	1.85	1.25-2.74
Male gender	0.39	0.30-0.53
TV in house (vs. no TV in house)	0.75	0.50-1.11
Dietary factors (unless otherwise stated, reference is no or occasional exposure)		
Cereal three or more times a week	1.16	0.86-1.56
Maize three or more times a week	1.33	0.95-1.85

Other environmental factors		
Paracetamol use at least once a month	1.45	1.11-1.89
House damp and wet inside (vs. not damp and wet)	1.58	1.09-2.29
Household member with TB ever (vs. no TB ever in household)	1.50	1.08-2.10

3.6 The "commuter group" and influence on these allergic symptoms

Those adolescents who commuted from low SES areas to schools in higher SES areas comprised a small proportion (1.7%) of the total population. The reference category was those students from low SES areas but who attended schools in their low SES area (n=1, 912). 48.2% (41) of the "commuters" reported rhinitis symptoms in the past year compared to 31.5% (603) of those students from the same low SES areas but attending local schools within the area. The differences were less for eczema symptoms, namely; 24.7% (21) of "commuters" and 25.9% (495) of those attending local schools. These prevalences were more suggestive when the more specific definitions of the allergic outcomes were applied. 27.0% (23) of the "commuters" reported allergic rhinitis symptoms compared to 18.0% (345) of those students from the same low SES areas but attending local schools within the area. For atopic eczema symptom reporting there were 15.3% (13) of "commuters" and 19.7% (376) of those attending local schools.

Table 9: Bivariate analysis: association of residence and school on all-cause and allergic outcomes

	All- cause rhinitis	**Allergic rhinitis**	**All-cause eczema**	**Atopic eczema**
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Reference category: low SES areas to low SES schools	1.00	1.00	1.00	1.00
"Commuters": low SES areas to high SES schools	2.18 (1.40-3.40)	1.33 (0.78-2.29)	0.71 (0.40-1.27)	0.76 (0.39-1.48)

High SES areas to high SES schools	1.66 (1.47-1.89)	0.95 (0.81-1.11)	0.48 (0.41-0.56)	0.40 (0.34-0.49)

The “commuters” appear to be at an increased odds for rhinitis (all-cause and allergic). For the outcome of eczema, the findings are suggestive of a protective effect; although to a lesser degree than the students from higher SES areas.

IV. DISCUSSION

The ISAAC Phase Three data analyses of the allergic rhinitis and atopic eczema outcomes reveal the following notable findings.

There were striking differences between allergic rhinitis and atopic eczema in the bivariate analyses as the predictors of allergic rhinitis – when assessed together with wheeze - suggest that, to a large extent, a higher social class (variables of language, maternal education and access to television) is a risk factor. The opposite was shown for atopic eczema, i.e., lower social class was found to be a predictor.

When reviewed individually, the final models of allergic rhinitis and atopic eczema demonstrate a mixture of biologic and class effects that are difficult to disentangle in such a study design. The final model of associations of those with comorbid symptoms confirms this statement.

This study found that there was a positive association between a primary school level of education of the mother and the symptoms of allergic rhinitis in multivariate analyses. The impact of parental education on health outcomes in children, especially those of an allergic nature, is a variable that has generated interest. The historical effect of limited and unequal access to education means that parental education can be used as a robust measure of SES in South Africa. The use of this variable in another country may therefore have different associations and implications. For example, Dom et al. (2009) have found that in Belgium, children with at least one highly educated parent tend to be more atopic than children with low-educated parents and that after adjustment for potential confounders, eczema in the child was positively associated (almost double the odds) with a high educational level of the parents.

The finding of this ISAAC analysis that maternal primary school level of education is a predictor of allergic rhinitis could be linked to an environmental marker of poverty, i.e. damp

condition of the house. The association between dampness and allergic rhinitis is discussed below.

For both allergic rhinitis and atopic eczema, male gender was found to be protective in this study. There is limited research on gender reporting of allergic symptoms. MacLean et al. (2010) found that although societal expectations for behaviour which translates to symptom reporting exist for both sexes, boys reacted to them as "rules" while girls took them to be as "guidelines". Therefore, while both felt pressurized to maintain composure in spite of physical or psychological symptoms, girls were more likely to consider seeking help if they were unwell than boys. Boys feared that their masculinity would be threatened were they to report any symptoms. Clough (2011) also links gender differences in disease to the hygiene hypothesis. Elements such as different societal norms of dressing (girls are more likely to be dressed in clothing that is not conducive for dirty play), cleanliness (the linking of dirt and immorality and standards for females "are generally higher") and parental supervision (parents are more likely to supervise the play of girls) could result in females being less exposed to microbial agents that stimulate the immune system, especially in a critical developmental period where the immune system may "benefit" the most from such exposure. The hormonal influences of oestrogen and progesterone may also be factors in the gender difference; they are noted to be immune-stimulatory while testosterone is anti-inflammatory (Osman 2007). Lastly, environmental exposures such as cigarette smoking and exposure to cosmetics that usually have their experimental phases at adolescence may exacerbate these gender differences (Osman 2007).

In the analysis of ISAAC Phase One data, Mercer et al. (2004) also reported that although the "commuters" (students resident in lower SES band attending schools in highest SES band) were a small sample (n=82 to 101), they had significantly higher prevalences of rhinitis and particularly eczema symptoms than the reference category (students resident in lower SES band attending schools in that same SES band). The previous findings as well as those of this study may be in keeping with the hygiene hypothesis as these students may be

"in transition" to a higher SES at home, and hypothetically to a cleaner environment, and thus may be more prone to allergic disease. However, lack of statistical power limited the conclusions that could be drawn.

In general, a clear picture of the effect of dietary exposures did not emerge for either outcome. The literature review suggested seafood, cereal, starch and fruits as protective factors (Ellwood 2001; Garcia-Marcos 2007). In this study, apart from cereal consumption, neither seafood nor fruit consumption demonstrated any significant association with either outcome. The multivariate analyses showed that only cereal intake 3 or more times a week was a significant risk factor. Mahlati (2007) found maize consumption to be protective and pasta consumption to be a risk factor for asthma symptom prevalence respectively. Pasta and maize consumption were a risk factor and also protective for atopic eczema respectively but these findings did not persist in multivariate analyses.

In summary, an important limitation of the core written questionnaire for the dietary component could be different cultural interpretations by the respondents. As with the range of fast food available, cereal in the questionnaire may be interpreted as breakfast with commercial brands (e.g. corn flakes) but could be only a slice of bread as well.

Damp housing was a risk factor for both outcomes. Batlles-Garrido et al. (2010) suggest that dampness may be related to dust mite sensitization as well as allergens known as *Alternaria* that proliferate in damp environments over time. *Alternaria* mould is present indoors and outdoors and are among the largest spores (>10 µm); and therefore capable of inducing allergic rhinitis as particles >10 µm are usually trapped in the upper airways (Randriamanantany 2010). The presence of *Alternaria* has been found to be an independent risk factor for allergic rhinitis (Randriamanantany 2010) which may be consistent with the dampness finding of this study.

Cooking with wood as a fuel was a risk factor for all-cause rhinitis but not statistically significant for allergic rhinitis. This is in keeping with the evidence that the wood effect is

more of an irritant nature than cause of more specific allergic rhinitis. The combustion of biomass fuels such as wood for cooking and/or heating releases pollutants that include carbon monoxide (CO), volatile organic compounds (VOCs) and nitrogen dioxide (NO2). Acute and chronic respiratory health effects have been linked to these indoor pollutants. A study in Bangladesh (Khalequzzaman 2007) that measured the concentrations of certain pollutants found a significant association between the use of biomass fuels and respiratory symptoms such as nasal discharge (adjusted OR range 4.0 to 6.3). Eczema and asthma failed to show an association with these fuels. However, the authors recognized that the health impact of such indoor pollutants was far less than that of SES which would confound the results.

More conclusive findings were from Padhi et al. (2008) – exposure to cooking smoke from biomass combustion was significantly associated with the prevalence of doctor-diagnosed asthma (OR = 2.20; 95% CI 1.16-4.19) and other respiratory symptoms in children. This effect was independent of factors such as age, maternal education and household living conditions.

Positive tuberculin reactivity has been found to be protective for allergic disease; either for both atopic eczema and rhinitis or either outcome (Shirakawa 1997; Steenhuis 2007; Miyake 2007). The association between a household member with a history of TB and both allergic outcomes is inexplicable. The social class effects of environmental influences as well as the timing of the mycobacterial inhibition of atopy in life (Soysal 2008) are factors to consider in the role that TB plays in allergic disease.

Lastly, paracetamol use at least once per month is a predictor of all three outcomes, including comorbid symptoms. There is biologic plausibility (Farquhar 2009) and the possibility of reverse causation may be less applicable as it was also a risk factor for the outcome of eczema (Beasley 2010).

However, Illi et al. (2004) showed a link between infantile atopic eczema and asthma (or bronchial hyper responsiveness) that may persist to adolescence. An evaluation of cohort data (Tapianinen 2010) found that adolescents with asthma or eczema at follow up had had more febrile days per person-year at risk (PYR) in childhood than healthy adolescents. Therefore, there may be an increased tendency for paracetamol administration amongst not only children with diagnosed allergic disease, but also those who had symptoms but did not consult a physician. Another prospective birth cohort (until 7 years of age) has shown a lack of association between use of paracetamol for non-respiratory tract infections and asthma, rhinitis and eczema outcomes (Lowe 2010). Since interventional study designs to address this association have substantial resource and ethical implications, it may be more appropriate to recognise that, despite the plausible biologic mechanisms, the benefits of paracetamol administration in children as an anti-pyretic outweigh those of alternative medications (e.g. non-steroidal anti-inflammatory) and its possible additional risk of allergic disease.

There are several limitations to consider in the interpretation of this study's findings. Firstly, interpretation of temporality associated with the cross-sectional study design is a limitation of the study. As noted for the paracetamol variable in particular, reverse causation is difficult to disprove in this type of design.

Whereas the use of a video questionnaire for asthma and wheeze reduced translation and cultural interpretation challenges in understanding these symptoms in the core written questionnaire, measurement bias was not able to be reduced for the rhinitis and eczema outcomes due to the lack of this component.

The lack of allergy testing in this study has meant that an assessment of atopic status was dependent on additional questions in the core written questionnaire that, without the aid of a visual component, are prone to misinterpretation by the respondent.

V. CONCLUSION

The analyses demonstrate that in general, the outcomes of allergic rhinitis and wheeze suggest findings in the same direction, i.e. of a positive socioeconomic gradient compared to atopic eczema, which suggests a negative socioeconomic gradient. The positive associations of high SES and allergic rhinitis lend support to the accepted understanding of the hygiene hypothesis, i.e. with more sanitized surroundings there is a loss of protective immune factors that were previously induced by exposure to microbial agents in food and the environment. The second notable finding of the "commuter" group (low SES resident students attending higher SES schools) and its increased odds of allergic rhinitis but protected from atopic eczema compared to those adolescents from the same residence but attending low SES schools, is also consistent with this hypothesis.

However, when each outcome is assessed on its own, a combination of high and low SES associations is shown; this is confirmed by the findings of the comorbid group.

The contribution of diet requires more context-specific research as the interpretation of the ISAAC questionnaire is very subjective.

The finding that male gender is protective for both allergic rhinitis and atopic eczema is consistent with research that show for biologic and socially-engrained reasons, females may be more likely to report general physical and psychological symptoms than males.

Lastly, even given the positive associations of paracetamol use at least once a month and all three allergic outcomes a study such as this cannot exclude reverse causation.

This is the first analysis of the Cape Town ISAAC data that has compared the determinants of rhinitis, eczema and wheeze symptoms amongst adolescents. In conclusion, it is hoped that this study has contributed to a better understanding of the determinants of allergic rhinitis and atopic eczema symptoms, and their relation to those of wheeze, amongst adolescents in South Africa, as well as pointing to lines of future investigation.

REFERENCES

Ait-Khaled, N., Pearce, N., Anderson, H.R., Ellwood, P., Montefort, S., Shah, J. and the ISAAC Phase Three Study Group. 2009, "Global map of the prevalence of symptoms of rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three" *Allergy*, vol. 64, pp.123–148.

Annesi-Maesano, I., Oryszczyn, M.P., Raherison, C. Kopferschmittz, C., Pauliz, G., Taytard, A., Tunon de Lara, M., Vervloetz, D., Charpinw, D. 2004, "Increased prevalence of asthma and allied diseases among active adolescent tobacco smokers after controlling for passive smoking exposure. A cause for concern?" *Clin Exp Allergy,* vol. 34, pp. 1017–1023.

Armentia, A., Banäuelos, C., Arranz, M.L., Del Villar, V., Martiân-Santos, J.M., Gil, F.J. M., Vega, J.M., Callejo, A., Paredes, C. 2001, "Early introduction of cereals into children's diets as a risk factor for grass pollen asthma" *Clinical and Experimental Allergy*, vol., 31, pp.1250 – 1255.

Asher, M.I. and Weiland, S.K on behalf of The Isaac Steering Committee. 1998, "The International Study of Asthma and Allergies in Childhood (ISAAC)" *Clinical and Experimental Allergy*, vol. 28, no. 5, pp. 52-66.

Asher, M.I., Keil, U., Ross Anderson, H., Beasley, R., Crane, J., Martinez, F., Mitchell, E.A., Pearce, N., Sibbald, B., Stewart, A.W., Strachan, D., Weiland, S.K., William, H.C. 1995, "International study of asthma and allergies in childhood (ISAAC): rationale and methods" *Eur Respir*, vol. 8, pp 483–491.

Asher, M.I., Montefort, S., Björkstén, B., Lai, C., Strachan, D., Weiland, S.K., William, H.C and the ISAAC Phase Three Study Group. 2006, "Worldwide time trends in the prevalence

of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys" *Lancet,* vol. 368, pp. 733–43.

Asher, M.I., Stewart, A.W., Mallol, J., Montefort, S., Lai, C., Aït-Khaled, N., Odhiambo, J.A., and the ISAAC Phase One Study Group. 2010, "Which population level environmental factors are associated with asthma, rhinoconjunctivitis and eczema? Review of the ecological analyses of ISAAC Phase One" *Respiratory Research,* vol. 11, no. 8.

Batlles-Garridoa, J., Torres-Borregob, J., Rubı´-Ruiza, T., Bonillo-Peralesa, A., .Gonza´lez-Jime´neza, Y., Mombla´n-DeCaboa, J., Aguirre-Rodrı´gueza, J., Losillas-Maldonadoa, A., Torres-Dazaa, M. 2010, "Prevalence and factors linked to allergic rhinitis in 10 and 11-year-old children in Almerıa. Isaac Phase II, Spain" *Allergol Immunopathol(Madr)*, vol. 38, no. 3, pp.135–141.

Beasley, R.W., Clayton, T.O., Crane, J., Lai, C., Montefort, S., von Mutius, E., Stewart, A. and the ISAAC Phase Three Study Group. 2010, "Acetaminophen Use and Risk of Asthma, Rhinoconjunctivitis and Eczema in Adolescents: Isaac Phase Three". Available: doi:10.1164/rccm.201005-0757OC [Accessed 18 Jan. 2011].

Bergmann, R.L., Edenharter, G., Bergmann, K.E., Wahn, V., Forster, J., Zepp, F., Wahn, U. 1998, "Atopic dermatitis in early infancy predicts allergic airway disease at 5 year" *Clin Exp Allergy*, vol. 28, pp. 965-70.

Bjorksten, B., Clayton, T., Ellwood, P., Stewart, A., Strachan, D. and the ISAAC Phase III Study Group. 2008, "Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase

III of the International Study of Asthma and Allergies in Childhood" *Pediatr Allergy Immunol*, vol. 19, pp.110–124.

Braback, L., Hjern, A., Rasmussen, F. 2005, "Social class in asthma and allergic rhinitis: a national cohort study over three decades" *Eur Respir J,* vol. 26, pp. 1064–1068.

Brenninkmeijer, E. E. A., Schram, M.E., Leeflang, M. M. G., Bos, J. D., Spuls, P. I. 2008, "Diagnostic criteria for atopic dermatitis: as systematic review" *British Journal of Dermatology*, vol. 158, no. 4, pp. 754-765.

Brunekeef, B., Stewart, A.W., Ross Anderson, H., Lai, C., Strachan, D., Pearce, N. And the ISAAC Phase 3 Study Group. 2009, "Self-reported truck traffic on the street of residence and symptoms of asthma and allergic disease: a global relationship in ISAAC Phase 3" *Environmental Health Perspectives*, vol. 117, no.11, pp. 1791-1798.

Clough, S. 2011, "Gender and the hygiene hypothesis" *Social Science & Medicine*, vol. 72, pp. 486 – 493.

Codispoti, C.D., Levin, L., LeMasters, G.K., Ryan, P., Reponen, T., Villareal, M., Burkle, J., Stanforth, S., Lockey, J.E., Khurana Hershey, G.K., Bernstein, D.I. 2010, "Breast-feeding, aeroallergen sensitization, and environmental exposures during infancy are determinants of childhood allergic rhinitis" *J Allergy Clin Immunol,* vol. 125, pp. 1054-60.

Cohet, C., Cheng,S., MacDonald, C., Baker, M., Foliaki, S., Huntington, N., Douwes, J., Pearce, N. 2004, "Infections, medication use, and the prevalence of symptoms of asthma, rhinitis, and eczema in childhood" *J Epidemiol Comm Health*, vol. 58, pp. 852-857.

Chalmers, D.A., Todd, G., Saxe, N., Milne, J.T., Tolosana, S., Ngcelwane, P. N., Hlaba, B.N., Mngomeni, L.N., Nonxuba, T. G., Williams, H. C. 2007, "Validation of the U.K. Working Party diagnostic criteria for atopic eczema in a Xhosa-speaking African population" *British Journal of Dermatology*, vol. 156, pp. 111–116.

Chatzi, L., Kogevinas, M. 2009, "Prenatal and childhood Mediterranean diet and the development of asthma and allergies in children" *Public Health Nutrition,* vol. 12, no.9A, pp. 1629–1634.

Czarnobilska, E., Obtulowicz, K., Dyga, W., Spiewak, R. 2010. "A half of schoolchildren with 'ISAAC eczema' are ill with allergic contact dermatitis". Available: doi: 10.1111/j.1468-3083.2010.03885.x [Accessed 17 Jan 2011].

Dom, S., Droste, J.H.J., Sariachvili, M.A., Hagendorens, M.M., Bridts, C.H., Stevens, W.J., Desager, K.N., Wieringa, M.H., Weyler, J.J. 2009, "The influence of parental educational level on the development of atopic sensitization, wheezing and eczema during the first year of life" *Pediatr Allergy Immunol,* vol. 20, pp. 438–447.

du Prel, X., Krämer, U., Behrendt, H., Ring, J., Oppermann, H., Schikowski, T., Ranft, U. 2006, "Preschool children's health and its association with parental education and individual living conditions in East and West Germany" *BMC Public Health*, vol. 6, pp. 312. Available: http://www.biomedcentral.com/1471-2458/6/312 [Accessed 29 March 2011]

Ellwood, P., Asher, M.I., Bjorksten, B., Burr, M., Pearce, N., Robertson, C. F. and the ISAAC Phase One Study Group. 2001, "Diet and asthma, allergic rhinoconjunctivitis and atopic

eczema symptom prevalence: an ecological analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data" *Eur Respir J*, vol. 17, pp. 436–443.

Ellwood, P., Asher, M.I., Beasley, R., Clayton, T.O., Stewart, A.W. and the ISAAC Steering Committee. 2005, "The International Study of Asthma and Allergies in Childhood: Phase Three rationale and methods" *Int J Tuberc Lung Dis*, vol. 9, pp. 10-16.

Eriksson, J., Ekerljung, L., Lotvall, J., Pullerits, T., Wennergren, G., Ronmark, E., Toren, K., Lundba, B. 2010, "Growing up on a farm leads to lifelong protection against allergic rhinitis" *Allergy*, vol. 65, pp. 1397–1403.

Farquhar, H., Crane, J., Mitchell, E.A., Eyers, S., Beasley, R. 2009, Editorial "The acetaminophen and asthma hypothesis 10 years on: A case to answer"*J Allergy Clin Immunol,* vol. 124, pp. 649-51.

Flohr, C., Weinmayr, G., Weiland, S.K., Addo-Yobo, E., Annesi-Maesano, I., Bjorksten, B., Braback, B., Buchele, G., Chico, M., Cooper, P., Clausen, M., El Sharif, N., Martinez Gimeno, A., Mathur,R. S., von Mutius, E., Morales Suarez-Varela, M., Pearce, N., Svabe, V., Wong, G.W.K., Yu, M., Zhong, N.S., Williams, H.C. and the ISAAC Phase Two Study Group. 2009, How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two" *British Journal of Dermatology*, vol. 161, pp. 846–853.

Garcia-Marcos, L., Canflanca, I.M, Batlles Garrido, J., Lopez-Silvarrey Varela, A., Garcia-Hernandez, G., Guillen Grima, F., Gonzalez-Diaz, C., Carvajal-Uruena, I., Arnedo-Pena, A., Busquets-Monge, R.M., Morales Suarez-Varela, M., Blanco-Quiros, A. 2007, "Relationship of asthma and rhinoconjunctivitis with obesity, exercise and Mediterranean diet in Spanish schoolchildren" *Thorax,* vol. 62, pp. 503–508.

Graham, N. 2005, “The relationship between socio-economic deprivation and asthma prevalence and severity in Cape Town adolescents” Unpublished (BSc Honours research project, Department of Environmental and Geographic Sciences, University of Cape Town)

Graham, N.M.H., Burrell, C.J., Douglas, R.M. 1990, “Adverse Effects of Aspirin, Acetaminophen, and Ibuprofen on Immune Function, Viral Shedding, and Clinical Status in Rhinovirus-Infected Volunteers” *The Journal of Infectious Diseases*, vol.162, pp. 1277-1282.

Guler, N., Kirerleri, E., Ones, U., Tamay, Z., Salmayenli, N., Darendeliler, F. 2004, “Leptin: Does it have any role in childhood asthma?” *J Allergy Clin Immunol*, vol. 14, pp. 254-9.

Haileamlak, A., Lewis, S.A., Britton, J., Venn, A.J., Woldemariam, D., Hubbard, R., Williams, H.C. 2005, “Validation of the International Study of Asthma and Allergies in Children (ISAAC) and U.K. criteria for atopic eczema in Ethiopian children” *British Journal of Dermatology*, vol. 152, pp. 735–741.

Haileamlak, A., Dagoye, D., Williams, H., Venn, A.J., Hubbard, R., Britton, J., Lewis, S.A. 2005, “Early life risk factors for atopic dermatitis in Ethiopian children” *J Allergy Clin Immunol*, vol. 115, no. 2, pp. 370-376.

Hetland, J., Torsheim, T., Aarø, L.E. 2002, “Subjective health complaints in adolescence: dimensional structure and variation across gender and age” *Scand J Public Health*, vol. 30, pp. 223-230.

Huang, S.L., Lin, K.C., Pan, W.H. 2001, “Dietary factors associated with physician-diagnosed asthma and allergic rhinitis in teenagers: analyses of the first Nutrition and Health Survey in Taiwan” *Clinical and Experimental Allergy,* vol. 31, pp. 259-264.

Ibargoyen-Roteta, N., Aguinaga-Ontoso, I., Fernandez-Benitez, M., Marin-Fernandez, B., Guillen-Grima, F., Serrano-Monzo, I., Hermoso-de-Mendoza, J., Brun-Sandiumetge, C., Ferrer-Nadal, A., Irujo-Andueza, A. 2007, "Role of the Home Environment in Rhinoconjunctivitis and Eczema in Schoolchildren in Pamplona, Spain" *J Investig Allergol Clin Immunol,* vol. 17, no.3, pp. 137-144.

Illi, S., von Mutius, E., Lau, S., Nickel, R., Gruber, C., Niggemann, B., Wahn, U and the Multicenter Allergy Study Group. 2004, "The natural course of atopic dermatitis from birth to age 7 years and the association with asthma" *J Allergy Clin Immunol,* vol. 113, pp. 925-31.

ISAAC Steering Committee. 1993, "International Study of Asthma and Allergies in Childhood Manual." Auckland, New Zealand/Münster, Germany: ISAAC

Jones, C.M. 2001, "Invited Commentary: "Race," Racism, and the Practice of Epidemiology" *Am J Epidemiol, v*ol. 154, no. 4, pp. 301-4.

Kajbaf, T.Z., Asar, S., Alipoor, M.R. 2011, "Relationship between obesity and asthma symptoms among children in Ahvaz, Iran: a cross sectional study" *Italian Journal of Pediatrics*, vol. 37, no.1. Available: doi:10.1186/1824-7288-37-1 [Accessed 17 Jan. 2011]

Khalequzzaman, M., Kamijima, M., Sakai, K., Chowdhury, N.A., Hamajima, N., Nakajima, T. 2007, "Indoor air pollution and its impact on children under five years old in Bangladesh" *Indoor Air,* vol. 17, pp. 297–304.

Lowe, A.J., Carlin, J.B., Bennett, C.M., Hosking, C.S., Allen, K.J., Robertson, C.F., Axelrad, C., Abramson, M.J., Hill, D.J., Dharmage, S.C. 2010, "Paracetamol use in early life and

asthma: prospective birth cohort study" *BMJ,* vol. 341:c4616. Available: doi:10.1136/bmj.c4616 [Accessed 15 March 2011].

MacLean, A., Sweeting, H., Hunt, K. 2010, "'Rules' for boys, 'guidelines' for girls: Gender differences in symptom reporting during childhood and adolescence" *Social Science & Medicine,* vol. 70, pp. 597–604.

Mahlati, U. 2007, "Dietary and environmental factors associated with symptoms or diagnosis of asthma in Cape Town school children: Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three Study" Unpublished (Thesis for MMed (Public Health), School of Public Health and Family Medicine, University of Cape Town)

Mercer, M.J., Joubert, G., Ehrlich, R.I., Nelson, H., Poyser, M.A., Puterman, A., Weinberg, E.G. 2004, "Socioeconomic status and prevalence of allergic rhinitis and atopic eczema symptoms in young adolescents" *Pediatr Allergy Immunol*, vol. 15, pp. 234–241.

Miyake, Y., Arakawaw, M., Tanaka, K., Sasaki, S., Ohya, Y. 2007, "Tuberculin reactivity and allergic disorders in schoolchildren, Okinawa, Japan" *Clinical and Experimental Allergy*, vol. 38, pp. 486–492.

Miyake, Y., Sasaki, S., Tanaka, K., Ohya, Y., Miyamoto, S., Matsunaga, I., Yoshida, T., Hirota, Y., Oda, H., and the Osaka Maternal and Child Health Study Group. 2007, "Fish and Fat Intake and Prevalence of Allergic Rhinitis in Japanese Females: the Osaka Maternal and Child Health Study" *Journal of the American College of Nutrition,* vol. 26, no. 3, pp. 279–287.

Myer, L., Ehrlich, R.I., Susser, E.S. 2004, "Social Epidemiology in South Africa" *Epidemiol Rev*, vol. 26, pp. 112-123.

Newson, R.B., Shaheen, S.O., Chinn, S., Burney, P.G.J. 2000, "Paracetamol sales and atopic disease in children and adults: an ecological analysis" *Eur Respir J*, vol. 16, pp. 817-823.

Nicolaou, N., Siddique, N., Custovic, A. 2005, "Allergic disease in urban and rural populations: increasing prevalence with increasing urbanization" *Allergy,* vol. 60, pp. 1357–1360.

Odhiambo, J.A., Williams, H.C., Clayton, T.O., Robertson, C.F., Asher, M.I. and the ISAAC Phase Three Study Group. 2009, "Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three" *J Allergy Clin Immunol*, vol. 124, pp.1251-8.

Okada, H., Kuhn, C., Feillet, H., Bach, J.F. 2010, "The 'hygiene hypothesis' for autoimmune and allergic diseases: an update" *Clinical and Experimental Immunology*, vol. 160, pp. 1–9.

Osman, M., Hansell, A.L., Simpson, C.R., Hollowell, J., Helms, P.J. 2007, "Gender-specific presentations for asthma, allergic rhinitis and eczema in primary care" *Primary Care Respiratory Journal*, vol. 16, no.1, pp. 28-35.

Padhi, B.K. and Padhy, P.K. 2008, "Domestic Fuels, Indoor Air Pollution, and Children's Health the Case of Rural India" *Ann. N.Y. Acad. Sci.*, vol. 1140, pp. 209–217.

Poyser, M.A., Nelson, H., Ehrlich, R.I. 2002, "Socioeconomic deprivation and asthma prevalence and severity in young adolescents" *Eur Respir J*, vol. 19, pp. 892- 898.

Pretoria: Statistics South Africa, 2005. "Census 2001: Primary tables Western Cape: Census '96 and 2001 compared". Available: *www.statssa.gov.za* [Accessed 17 Jan 2011]

Provincial Government of the Western Cape: Department of Health. 2010, "Annual Performance Plan 2010/11."

Prymula, R., Siegrist, C.A., Chlibek, R., Zemlickova, H., Vackova, M., Smetana, J., Lommel, P., Kaliskova, E., Borys, D., Schuerman, L. 2009, "Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials" *Lancet*, vol. 374, pp. 1339–50.

Quek, Y.W., Sun, H.L., Ng, Y.Y., Lee, H.S.,Yang, S.F., Ku, M.S., Lu, K.H., Sheu, J.N., Lue K.H. 2010, "Associations of serum leptin with atopic asthma and allergic rhinitis in children" *Am J Rhinol Allergy*, vol. 24, pp. 354–358.

Randriamanantany, Z.A., Annesi-Maesano, I., Moreau, D., Raherison, C., Charpin, D., Kopferschmitt, C., Lavaud, F., Taytard, A., De Blay, F., Caillaud, D. 2010, "Alternaria sensitization and allergic rhinitis with or without asthma in the French Six Cities study" *Allergy,* vol. 65, pp. 368–375.

Spergel, J.M., Paller, A.S. 2003, "Atopic dermatitis and the atopic march" *J Allergy Clin Immunol,* vol. 112 (suppl), pp. S118-27.

Soysal, A., Bahceciler, N., Barlan, I., Bakir, M. 2008, "Lack of an inverse association between tuberculosis infection and atopy: By T-cell-based immune assay (RD1–ELISpot)" *Pediatr Allergy Immunol,* vol. 19, pp. 709–715.

Steenhuis, T.J., van Aalderen, W.M.C., Bloksma, N., Nijkamp, F.P., van der Laag, J., van Loveren, H., Rijkers, G.T., Kuis, W., Hoekstra, M.O. 2007, "Bacille–Calmette–Guerin vaccination and the development of allergic disease in children: a randomized, prospective, single-blind study" *Clinical and Experimental Allergy*, vol. 38, pp. 79–85.

Strachan, D.P., Sibbald, B., Weiland, S.K., Ait-Khaled, N., Anabwani, G., Anderson, H.R., Asher, M.I., Beasley, R., Bjorksten, B., Burr, M.L., Clayton, T., Crane, J., Ellwood, P., Keil, U., Lai, C.K.W., Mallol, J., Martinez, F.D., Mitchell, F.A., Montefort, S., Pearce, N., Robertson, C.F., Shah, J.R., Stewart, A.W., von Mutius, F., Williams, H.C. 1997, "Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC)" *Pediatr Allergy Immunol*, vol. 8, pp.161-176.

Strachan, D.P., Cook, D.G. 1998, "Parental smoking and allergic sensitisation in children" *Thorax,* vol. 53, pp.117–123.

Strina, A., Barreto, M.L., Cunha, S., de Oliveira, M., Moreira, S.C., Williams, H.C., Rodrigues, L.C. 2010, "Validation of epidemiological tools for eczema diagnosis in Brazilian children: the ISAAC's and UK Working Party's criteria" *BMC Dermatology*, vol. 10, no.11. Available: http://www.biomedcentral.com/1471-5945/10/11 [Accessed 17 Jan. 2011]

Su, J.C., Kemp, A.S., Varigos, G.A., Nolan, T.M. 1997, “Atopic eczema: its impact on the family and financial cost” *Archives of Disease in Childhood*, vol. 76, pp. 159–162.

Sweeting, H., West, P. 2003, “Sex differences in health at ages 11, 13 and 15” *Social Science & Medicine,* vol. 56, pp. 31–39.

Tapiainen, T., Dunder, T., Mottonen, M., Pokka, T., Uhari, M. 2010. Letter to the Editor: “Adolescents with asthma or atopic eczema have more febrile days in early childhood: A possible explanation for the connection between paracetamol and asthma?” *J Allergy Clin Immunol,* vol., 125, no. 3, pp. 751-752.

Torres-Borrego, J., Molina-Terán, A.B. and Montes-Mendoza, C. 2008, “Prevalence and associated factors of allergic rhinitis and atopic dermatitis in children” *Allergol Immunopathol*, vol. 36, no. 2, pp. 90-100.

Vlaskia, E., Stavricb, K., Isjanovskac, R., Seckovaa, L., M. Kimovskaa, M. 2006, “Overweight hypothesis in asthma and eczema in young adolescents”, *Allergol et Immunopathol,* vol. 34, no. 5, pp. 199-205.

Weiland, S.K., von Mutius, E., Hüsing, A., Asher, M.I. on behalf of the ISAAC Steering Committee. 1999, “Intake of trans-fatty acids and prevalence of childhood asthma and allergies in Europe” *The Lancet*, vol. 353, pp. 2040-1.

Weiland, S.K., Bjorksten, B., Brunekeef, B., Cookson, W.O.C., von Mutius, Strachan, D.P and International Study of Asthma and Allergies in Childhood Phase II Study Group. 2004,

"Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods" *Eur Respir J*, vol. 24, pp. 406–412.

Wickens, K., Barry, D., Friezema, A., Rhodius, R., Bone, N., Purdie, G., Crane, J. 2005, "Fast foods – are they a risk factor for asthma?" *Allergy,* vol. 60, pp. 1537–1541.

Williams, H., Robertson, C., Stewart, A., Ait-Khaled, N., Anabwani, G., Anderson, H.R., Asher, M.I., Beasley, R., Bjorksten, B., Burr, M.L., Clayton, T., Crane, J., Ellwood, P., Keil, U., Lai, C.K.W., Mallol, J., Martinez, F.D., Mitchell, F.A., Montefort, S., Pearce, Shah, J.R., Sibbald, B., Strachan, D., von Mutius, F., Weiland, S.K.1999, "Worldwide variations in the prevalence of symptoms of atopic eczema in the international study of asthma and allergies in childhood" *J Allergy Clin Immunol*, vol. 103, pp.125-38.

Williams, H. and Flohr, C. 2006, "How epidemiology has challenged 3 prevailing concepts about atopic dermatitis" *J Allergy Clin Immunol*, vol. 118, pp. 209-13.

Williams, H., Stewart, A., von Mutius, E., Cookson, H. Ross Anderson, H. and the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One and Three Study Groups. 2008, "Is eczema really on the increase worldwide?" *J Allergy Clin Immunol,* vol. 121, pp. 947-54.

Zar, H.J., Ehrlich, R.I., Workman, L., Weinberg, E.G. 2007, "The changing prevalence of asthma, allergic rhinitis and atopic eczema in African adolescents from 1995 to 2002" *Pediatr Allergy Immunol*, vol. 18, pp. 560-565.

Appendix I

Appendix 1A: Instructions for authors – Journal of Allergy and Clinical Immunology

Official Journal of the American Academy of Allergy, Asthma and Immunology

Editor in Chief **DONALD Y. M. LEUNG, MD, PhD**

Managing Editor **GEORGE WOODWARD**

Senior Journal Manager **LAURA DINKINS-WHITE**

A. Original articles. These should describe fully, but as concisely as feasible, the results of original clinical and/or laboratory research. The average Original article fills 7 pages in the printed journal, although manuscripts that exceed this may be occasionally accepted for publication at the Editors' discretion. In general, an Original article should not exceed 3500 words, not including the abstract, figure legends, and references. Abstracts should be 250 words or less. If possible, each figure legend should be held to 60 words or less. Each Original article may be accompanied by no more than 8 graphic presentations (tables and/or figures)— for example, 3 tables + 5 figures. (Additional text, tables, or figures can be designated as "supplemental" material, which will be included in the JACI's Online Repository. For more on this option, please see the "Online Repository Materials" section below.) Please note: Original article manuscripts that are determined to significantly exceed these limits may be returned to the authors for shortening prior to review. The manuscript should be organized in the order listed below. ***Failure to follow this format may result in the manuscript being returned to the author(s) for revision prior to review.***

The title page, abstract, Capsule Summary, key words, abbreviations, text, acknowledgments, references, tables and figure legends should be included in one word-processing file (in .doc or .wpd format). Figures should be loaded as separate files in the format specified below.

1. *Title page.* The title of an article is the first exposure that an editor, reviewer, or reader will

have to your work's purpose and significance. Additionally, accurate indexing and abstracting of scientific articles depend on a clearly written title that conveys the key message of the paper. Thus, the title is the most important phrase in a paper and should inform and convince the potential reader that the article is important enough to read. Refer to the suggestions that follow to develop a title that is effective and appealing.

- Keep the title simple, clear, specific, and succinct.
- Keep the title succinct: Limit it to 12 words or fewer.
- Aim for a title that can be quickly scanned and understood by the reader.
- Communicate a single subject or idea in the title.
- Construct the title around the article's key words.
- Picture the target audience and use terms and key words that are clear to and familiar to that group.
- Eliminate all nonessential words and details; do not include information about objectives and methods.
- Ask yourself these questions: Does the title capture/pinpoint what this paper is about? Does it inform adequately?
- Include the specific symptom, condition, intervention, mechanism, or function of the paper's central focus.
- Mention any defining population, age, gender, or animal species that distinguishes the work.
- Use accurate English and correct, simple word order.
- Use terms that are specific rather than general (e.g., "penicillin" rather than "betalactam antibiotic") and include terms that clarify (e.g., "CXCR4" rather than "chemokine receptors").
- Avoid using strong words (such as "robust," "innovative," "significant," "vigorous," and "aggressive"), as they may suggest exaggerated or unwarranted claims.
- Use wit carefully and appropriately; be informative first and clever second. Although a

universally understood pun can work well to attract interest, ensure that it will not confuse or mislead the reader.

- Finalize the title after completing the manuscript: review the title after any revisions to ensure that it still communicates the paper's core message.

The title should be followed by:

- The list of authors, including their full names, highest academic degrees, and institutional affiliations. Restrict the list of authors to those who have made material contributions to the research and who contributed to the writing and review of the manuscript.
- The name, address, telephone number, fax number, and e-mail address of the author who should be contacted regarding reprint requests or other correspondence received in the Editorial Office regarding the manuscript.
- A declaration of all sources of funding. Authors are required to disclose any financial relationship with a biotechnology and/or pharmaceutical manufacturer that has an interest in the subject matter or materials discussed in the submitted manuscript.
- A total word count, which includes the number of words in the *body* of the manuscript (Introduction through Discussion only); the abstract should not be included in the count. Figure and table legends are included in the estimation of the overall space required for figures and tables, so they should not be counted here.

2. *Abstract.* As a general rule, the abstract should be **no longer than 250 words.** It should summarize the results and conclusions concisely. Tabular data should not be included and acronyms/abbreviations should be avoided or spelled out fully. Abstracts should be structured as follows:

- **Background:** What is the major problem that prompted the study?
- **Objective:** What is the purpose of the study?
- **Methods:** How was the study done?
- **Results:** What are the most important findings?
- **Conclusion:** What is the most important conclusion drawn?

3. Clinical Implications or Key Messages. Provide ONE of the following:

either

• a very brief paragraph (consisting of no more than 30 words) summarizing the diagnostic, therapeutic, or management implications of the article.

The heading for this paragraph should be **Clinical Implications.**

or

• (if the article is mechanistic) two or three independent bulleted statements that present the key findings or concepts in the article and perhaps comment on their implications. The heading for this small set of bulleted statements should be **Key Messages.**

4. *Capsule summary.* The Table of Contents entry for each Original Article published in the Journal includes a short summary that encapsulates the report's findings for a clinically oriented audience. To create this summary, the authors must compose one or two brief sentences (totaling no more than 35 words) that describe the article's contribution to the literature. These sentences should succinctly state why the article is important and compelling and what relevance it has for the clinician.

5. *Key words.* A list of up to ten key words should follow the Capsule Summary.

6. *Abbreviations.* Provide a list of any abbreviations/acronyms (and their definitions) on a separate page following the key words. Only standard abbreviations are to be used. Consult *Scientific Style and Format* by the Council of Biology Editors or the AMA's *Manual of Style*. A laboratory or chemical term or the name of a disease process that will be abbreviated must be spelled out at first mention, the acronym or abbreviation following in parentheses.

Please note: Abbreviations in the title and abstract are not acceptable. Even if they are included in the list of abbreviations, they should be spelled out in those locations.

7. *Text.* The manuscript should be written in clear and concise English. Authors whose primary language is not English should obtain assistance with writing to avoid grammatical problems. **The text should be organized in sections as follows: *Introduction, Methods, Results*, and *Discussion*.** Each section should begin on a new page.
The generic terms for all drugs and chemicals should be used.

In studies involving human subjects, a statement describing approval by the appropriate Institutional Review Board is required. Studies involving experimental animals must include a statement in the Methods section indicating which guidelines were followed for the care and use of the animals (e.g., the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research or the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press [revised 1996]).

8. *Acknowledgments.* General acknowledgments for consultations, statistical analyses, and the like should be listed at the end of the text, including full names of individuals involved.

However, acknowledgment of funding should be listed on the title page.

9. *References.* It is the Editors' expectation that authors will perform a comprehensive search of the literature to gather the most current articles relative to the subject matter. All references that are five years old or more should be replaced with current literature, unless the referenced publication is a classic work that underscores the core subject.

References should follow "Vancouver style."

See http://www.nlm.nih.gov/bsd/uniform_requirements.html for more information. Manuscripts in preparation, personal communications, and other unpublished information should *not* be cited in the reference list but may be mentioned in the text in parentheses. The references must be identified in the text by superscript Arabic numerals and numbered in consecutive order as they are mentioned in the text. The list of references, in numeric sequence, should be typed at the end of the article. Typing of the references is preferred over the use of your word processing program's footnote or endnote feature (or a program such as EndNote or Reference Manager) to create citations. If you do use EndNote, please remove the links between the reference number and the citations by taking the following steps: (1) Using the "Select All" feature (Ctrl-A for PCs. Cmd-A for MACs), highlight the entire text of the file, including the references. (2) Use the keystroke command "Ctrl-6" for PCs of "Cmd-6" for MACs. (3) Save.

This will remove the links (permanently) without disturbing the reference numbers or the citations. It is recommended that you save one copy of your manuscript with the EndNote links in place (for your reference) and one copy of your manuscript without the EndNote links (for submission purposes).

Please note that inclusive page numbers are required. List all authors' names when there are six or fewer; when there are seven or more, list the first six and add "et al."

Formatting of Articles

Basic Formatting

Be sure the entire manuscript (all text, legends, captions, etc.) is in a standard font such as Times New Roman, Arial, or Courier, size 12. All sections, including references, should be double-spaced, with margins of at least one inch on all sides. On each page, the last name of the first author and the page number should appear in the upper right corner. Begin numbering with the title page as page 1. Be sure to display line numbers (1, 2, 3, and so forth) in the left margin of the manuscript. (Line numbering can be added from the Page Setup or Format menu of word processing programs.) The line numbering should be continuous throughout the entire manuscript, from the title page through final page (i.e., do not begin numbering from 1 again at the top of each page).

Graphic Presentations

The total number of graphic presentations (tables and/or figures) per manuscript should be no greater than 8 (examples: 8 tables + 0 figures; 5 tables + 3 figures; 2 tables + 6 figures; 0 tables + 8 figures).

A. Tables. If tables appear in the manuscript, they must be included in the electronic submission. They may be placed within the manuscript file or loaded as separate files (in .doc or .wpd format). Tables should supplement, not duplicate, the text; they should be on separate pages, one table per page, and should be self-explanatory and numbered with Roman numerals in order of mention. A brief title should be provided directly above each table. Any text within the table should be in Times New Roman font. Any abbreviations should be defined at the bottom of the table. When creating a table, use the word-processing program's table formatting feature; otherwise, use only tabs (not spaces) to align columns. Glossy prints and reduced versions of typewritten tables are unacceptable. The table

number should appear in the electronic file. The maximum size for a table is ½ page. The maximum number of graphic presentations (tables and/or figures) per manuscript is 8 (examples: 8 tables + 0 figures; 5 tables + 3 figures; 2 tables + 6 figures; 0 tables + 8 figures).

B. Figure legends. Figure legends should be typewritten, double-spaced, and listed on a separate page after the tables. They should not appear on the figures. The figure legend will be included when sizing the figure and its length must therefore be taken into consideration. The figure title should appear at the beginning of each legend. The legends themselves should be succinct (no more than 60 words), identifying the data or subject being presented, but explaining methods or results. Do not place titles or legends within the figures.

C. Figures. If illustrations appear in the manuscript, they must be submitted in electronic format along with the rest of the manuscript. Each figure should be submitted as a separate electronic file, and should not be inserted into the file containing the text of the manuscript. Complete instructions for online submission are available in the "Tutorial for Authors" at the EES Web site http://ees.elsevier.com/jaci/). The maximum number of graphic presentations (tables and/or figures) per manuscript is 8 (examples: 8 figures + 0 tables; 6 figures + 2 tables; 3 figures + 5 tables; 0 figures + 8 tables).

Online Repository Materials

The Journal will consider posting ancillary materials (non-essential tables, figures, appendices, questionnaires, etc.) in an Online Repository (OR) on the JACI Web site (http://www.jacionline.org). The OR is for peer-reviewed material that cannot be included in the print version of an article due to space considerations. The Editor and reviewers are able to review material proposed for the OR. Readers of the Journal's print version will be directed to the OR for reference. Note: OR material consisting of 15 pages or less is built

directly into the downloadable PDF of the manuscript.

On an individual basis, the Editors will determine whether ancillary material submitted in support of a manuscript is warranted. In some instances, an Editor may suggest when requesting a revision that part of the data be presented for the OR and removed from the manuscript, perhaps at the request of the reviewers. In both cases, authors should include a cover letter to the Editor, indicating the material to be considered for the OR and justifying its inclusion.

The ancillary material must be submitted in EES simultaneously with the rest of the manuscript. The OR material should be loaded as separate files, and should follow the end of the regular manuscript. For revisions that will include newly designated OR material, the Marked Manuscript should show where materials were removed from the original version, and include appropriate statements directing readers of the article in the print journal to the OR. The Unmarked Manuscript will reflect the latter changes. For more complete instructions, see the "Tutorial for Authors" at the EES Web site (http://ees.elsevier.com/jaci/).

Online Repository materials must be accompanied by a separate title page that includes the heading "Online Repository," all author names and their affiliations, and contact information for the corresponding author. All text files for the OR should be formatted per directions for regular manuscript materials (see section A). Tables for the OR should be submitted as files with any of the following extensions: .pdf, .csv, .txt, .doc, .rtf, .xls, .ppt. Figures for the OR do not need to conform to the print specifications for resolution, but they do need to appear clear and crisp when viewed electronically. PowerPoint files may be used. Figures and Tables must be labeled with unique designations as Figure E1, Table E1, etc. Similarly, if citations are made within the ancillary material, a list of references, separate from the manuscript's references, must be included and labeled E1, E2, etc. Authors may repeat sentences or references in the OR that are included in the manuscript, if necessary for reader comprehension. In the manuscript text, materials that are housed in the Online

Repository must be referenced specifically ("see Figure E1 in the Online Repository"). It is important to remember that material for the OR is independent from the manuscript and will appear online only.

Appendix 1B: Ethics approval letter

UNIVERSITY OF CAPE TOWN

Research Ethics Committee
Faculty of Health Science
Anzio Road, Observatory, 7925
Queries : Xolile Fula
Tel : (021) 406-6492 Fax: 406-6390
E-mail : Xfula@curie.uct.ac.za

01 August 2001

REF REC: 203/2001

Dr H. Zar
Paediatrics

Dear Dr Zar

THE INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD (ISAAC0 PHASE THREE IN CAPE TOWN, SOUTH AFRICA

Thank you for submitting your study to the Research Ethics Committee for review.

It is a pleasure to inform you that the Committee has formally approved your study.

Please quote the above REC reference number in all correspondence

Attached is a copy of the list of members who attended the meeting.

Yours sincerely

PROFESSOR CR SWANEPOEL
CHAIRPERSON

Appendix 1C: Consent form for parents

Dear Parent/Guardian

We are inviting your child to take part in an important survey about child health with the approval of your school. First, your child will be asked to complete a questionnaire on breathing, nose and skin problems. Then a 7 minute video about exercise and breathing will be shown and your child will be asked to complete a further questionnaire. The survey will take up to 40 minutes of class time, and will be done during a suitable class period.

This survey is being carried out in randomly selected schools in Cape Town and also in many overseas countries including Australia, Canada, USA, Britain, Kenya and Germany.

We ask you to consider this information sheet, and if you agree to your child taking part in the survey, then please sign below. Your child's questionnaire will be treated confidentially, only a code number will be entered in the computer.

This survey has the approval of your child's Principal and teachers. It also has the approval of the University of Cape Town's Ethics and Research Committee and the Department of Education and Culture.

If there is any further information you require about the survey, please contact me at telephone: **685-4103**.

Yours sincerely

Dr Heather Zar

Principal Investigator

- -

Please return this section to school with your child:

I agree to allow my child to take part in a survey on breathing, nose and skin problems.

Signed . . . . . Parent's Name: . . . . . .

Date: . . . . . Child's Name: . . . . . .

Appendix 1D: Consent form for children

CONSENT FORM FOR CHILDREN AGED 13 TO 14 YEARS: Cape Town Survey of Breathing, Nose and Skin Problems in Children: Phase Three

We are inviting you and the other children in your class to take part in an important study to understand more about the increasing problem of breathing, nose and skin problems in children. Many schools in Cape Town took part in a similar study in 1995, and your school has been selected to participate in this study. This study is being carried out in a number of schools in Cape Town and in many overseas countries.

We will ask you to complete a written questionnaire and to watch a video about exercise and breathing which lasts about ten minutes. The survey will take about 60 minutes and will be done during a school period. This study has been approved by the Ethics Committee of the University of Cape Town. If you have questions or require further information about the study, you can discuss these with a member of our research team when they visit your school. You may choose not to participate if you do not want to.

Thank you.

Dr Heather Zar

Principal Investigator

I, _____(name) agree to participate in the survey on respiratory and skin problems in children.

Signed: _____

Date: _____

Appendix 1E: Questionnaire (English version)

SURVEY OF BREATHING, NOSE AND SKIN PROBLEMS

Office Use Only | | | | | | | | |

V. Instructions for completing the questionnaire

On this sheet are questions about your name, address, and birth date. Please write in your answers to these questions in the space provided.

All other questions require you to TICK your answer in a box or WRITE the answer in a box. If you make a mistake **put a cross** in the box and tick the correct answer. **Only mark one option.**

Examples of how to mark questionnaires: Age [13] years

	Yes	No
To answer Yes/No, put a tick in the appropriate box as per example	☐	✔

Your name:

School:

Home address:

Today's date:

	Day	Month	Year
Your age:	☐		
	years		
Your date of birth:	☐	☐	☐
	Day	Month	Year

	Boy	Girl
Are you:	☐	☐

Were you born in Cape Town?	Yes ☐	No ☐
If you were not born in Cape Town, how old were you when you came to Cape Town?	☐	Years

	Yes	No
1. Have you ever had wheezing or whistling in the chest at any time in the past?	☐	☐

1. IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

	Yes	No
2. Have you had wheezing or whistling in the chest in the past 12 months?	☐	☐

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

---

3. How many attacks of wheezing have you had in the past 12 months?

None	1 to 3	4 to 12	More than 12
☐	☐	☐	☐

4. In the past 12 months, how often, on average, has your sleep been disturbed due to wheezing?

Never woken up with wheezing	Less than one night per week	One or more nights per week
☐	☐	☐

	Yes	No
5. In the past 12 months, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?	☐	☐
6. Have you ever had asthma?	☐	☐

	Yes	No
7. In the past 12 months, has your chest sounded wheezy During or after exercise?	☐	☐

	Yes	No
8. In the past 12 months, have you had a dry cough at night, Apart from a cough associated with a cold or chest infection?		

ALL QUESTIONS ARE ABOUT PROBLEMS THAT OCCUR WHEN YOU DO NOT HAVE A COLD OR THE FLU

	Yes	No
9. Have you ever had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu?	☐	☐

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 14

	Yes	No
10. In the past 12 months, have you had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu?	☐	☐

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 14

	Yes	No
11. In the past 12 months, has this nose problem been accompanied by Itchy-watery eyes?	☐	☐

12. In which of the past 12 months Did this nose problem occur? (Please tick any which apply)

January ☐	February ☐	March ☐	April ☐
May ☐	June ☐	July ☐	August ☐
September ☐	October ☐	November ☐	December ☐

13. In the past 12 months, how much did this nose problem interfere With your daily activities?

Not at all ☐	A little ☐	A moderate amount ☐	A lot ☐

	Yes	No
14. Have you ever had hayfever?	☐	☐

	Yes	No
15. Have you ever had an itchy rash which was coming And going for at least six months?	☐	☐

2. IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 20

	Yes	No
16. Have you had this itchy rash at any time in the past 12 months?	☐	☐

3. IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 20

	Yes	No
17. Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?	☐	☐
18. Has this rash cleared completely at any time during the past 12 months?	☐	☐

19. In the past 12 months, how often, on average, have you been kept awake at night by this itchy rash?

Never in the past 12 months	Less than one night per week	One or more nights per week
☐	☐	☐

	Yes	No
20. Have you ever had eczema?	☐	☐

STOP HERE.

PLEASE GET YOUR WEIGHT AND HEIGHT FILLED IN BEFORE CONTINUING.

1. Weight: ☐ kg

2. Height: ☐ centimetres

3. In the past 12 months, how often, on average, did you eat or drink the following?: (Please leave blank if you do not know what the food is)

	Never or rarely	Once or twice per week	Three or more times a week
Meat (e.g. beef, lamb, chicken, pork)	☐	☐	☐
Seafood (including fish)	☐	☐	☐
Fruit	☐	☐	☐
Vegetables (all types)	☐	☐	☐
Peas, beans	☐	☐	☐
Cereal (including bread)	☐	☐	☐
Maize (Mielie meal)	☐	☐	☐

Pasta	☐	☐	☐
Rice	☐	☐	☐
Butter	☐	☐	☐
Margarine	☐	☐	☐
Nuts (including Peanuts)	☐	☐	☐
Potatoes	☐	☐	☐
Milk	☐	☐	☐
Eggs	☐	☐	☐
Fast food/burgers	☐	☐	☐

4. How many times a week do you have enough exercise or physical effort to make you breathe hard?:

Never or occasionally ☐

Once or twice per week ☐

Three or more times a week ☐

5. During a normal week, how many hours a **day** do you watch television?:

Less than 1 hour ☐

1 hour but less than 3 hours ☐

3 hours but less than 5 hours ☐

5 hours or more ☐

6. In your house, what fuel is usually used for cooking?:

Electricity ☐

Gas ☐

Paraffin ☐

Wood (including open fires) ☐

Other - Please specify ☐

7. In your house, what fuel is usually used for heating?:

Electricity ☐

Gas ☐

Paraffin ☐

Wood (including open fires) ☐

Other - Please specify ☐

8. In the past 12 months, how often, on average, have you taken Panado?:

Never ☐

At least once a year ☐

At least once per month ☐

9. How many **older** brothers and sisters do you have?: ☐ brothers and sisters

10. How many **younger** brothers and sisters do you have?: ☐ brothers and sisters

11. Were you born in South Africa?:

Yes ☐

No ☐

12. How many years have you lived in South Africa?: ☐ years

13. What level of education has your mother reached or completed?:

Primary school ☐

High school ☐

College, university or other form of tertiary education ☐

14. What level of education has your father reached or completed?:

Primary school ☐

High school ☐

College, university or other form of tertiary education ☐

15. How often do trucks pass along the street where you live, on weekdays?

Never ☐

Seldom ☐

Frequently through the day ☐

16. In the past 12 months, have you had a cat in your home?:

Yes ☐

No ☐

17. In the past 12 months, have you had a dog in your home?

Yes ☐

No ☐

18. Does your mother (or female care giver) smoke cigarettes?:

Yes ☐

No ☐

19. Does your father (or male care giver) smoke cigarettes?:

Yes ☐

No ☐

20. How many people living in your house smoke cigarettes?: ☐ people

21. Do you smoke cigarettes?:

Yes ☐

No ☐

22. Is your house damp or wet inside?:

Yes ☐

No ☐

23. Has anyone in your household ever had TB?:

Yes ☐

No ☐

24. Have you ever been treated for TB?:

Yes ☐

No ☐

25. How many people live in your house?:

Adults ☐

Children ☐

26. Do you have taps for running water in your house?:

Yes ☐

No ☐

27. Do you have electricity in your house?:

Yes ☐

No ☐

28. Do you have a TV in your house?:

Yes ☐

No ☐

29. What type of home do you have?:

House ☐

Flat ☐

Shack ☐

Other ☐

30. How many people living in your household have regular jobs?: ☐ people

31. How many people living in your household are unemployed and looking for work?: ☐ people

32. How many people share your bedroom at night?: ☐ people

STOP HERE.

PLEASE WAIT FOR THE VIDEO TO START BEFORE COMPLETING THE NEXT SECTION OF THE QUESTIONNAIRE.

	Yes	No
1. Has your breathing been like this at any time in your life?	☐	☐
If YES, has this happened in the last year?	☐	☐
If YES, has this happened one or more times a month?	☐	☐

	Yes	No
2. Has your breathing been like the boy's in the **dark** shirt following exercise at any time in your life?	☐	☐

If YES, has this happened in the last year?		
If YES, has this happened one or more times a month?		

	Yes	No
3. Have you been woken like this at night, at any time in your life?		
If YES, has this happened in the last year?		
If YES, has this happened one or more times a month?		

	Yes	No
4. Have you been woken at night like this, at any time in your life?		
If YES, has this happened in the last year?		
If YES, has this happened one or more times a month?		

	Yes	No
5. Has your breathing been like this, at any time in your life?		
If YES, has this happened in the last year?		
If YES, has this happened one or more times a month?		

Appendix 1F: Questionnaire (Xhosa version)

Uphando lweengxaki zokuphefumla, impumlo nolusu

Isetyenziswa yi-ofisi kuphela | | | | | | | | |

VI. Imiyalelo yokuphendula imibuzo wkiphepha lemibuzo

Kweli phepha yimibuzo malunga negama lakho, Idilesi yasekhaya, umhla wokuzalwa. Nceda bhala iimpendulo zale mibuzo kwisikhewu esinikiweyo.

Yonke eminye imibuzo ifuna **uphawule impendulo yakho okanye ubhale kwi bhokisi**. Xa wenze impazamo **Hlaba** kwibhokisi uze ufake uphawu olulungileyo kwimpendulo echanekileyo kuwe.

Imizekelo yokuphawula impendulo : Iminyaka ☐ **Iminyaka**

Ukuphendula Ewe okanye hayi Faka uphawu — Ewe ☐ Hayi ☐

Kwibhokisi eyiyo

Igama lakho: ☐

Isikolo Sakho: ☐

Idilisi Yasekhaya: ☐

☐

☐

Umhla namhlanje: ☐ ☐ ☐

Usuku Inyanga Unyaka

Ubudala bakho:

Iminyaka

Umhla wokuzalwa:

Umhla Inyanga Unyaka

Uyi: Nkwekwe Intombazana

Wazalelwa e-Kapa? Ewe Hayi

Ukuba akuzalwanga e-Kapa ufike uminyaka, mingaphi E-Kapa ? Yeminyaka

1. Wakha wanaso isifuba esishinyeneyo okanye esiminxeneyo nanini na ngaphambili?

Ewe ☐ Hayi ☐

4. Ukuba uphendule "hayi" nceda tsibela kumbuzo 6

---

2. Wakha wanaso isifuba esishinyeneyo kwezi nyanga zili-12 zigqithileyo?

Ewe ☐ Hayi ☐

Ukuba uphendule "hayi" nceda tsibela kumbuzo 6

---

3. Uhlaselwe kangaphi kwezi nyanga zili-12 zigqithileyo sisifuba esishinyeneyo?

Zange ☐ 1 kuye 3 ☐ 4 kuye 12 ☐ Ngaphezu 12 ☐

4. Kwiinyanga ezili-12 ezigqithileyo uphazanyiswe kangaphi ubuncinane kubuthongo bakho kukuminxana kwesifuba?

Zange ndivuswe sisifuba esitswinayo ☐ Ngaphantsi kobusuku obunye ngeveki ☐ Kanye nangaphezulu ngeveki ☐

5. Kwiinyanga ezili-12 ezigqithileyo,Kwakha kwanzima ukutswina kwesifuba kangangokuba kunqumle ukuthetha kwakho de ubize igama libe linye ngexesha uzama ukuphefumla?

Ewe ☐ Hayi ☐

6. Wakha wanayo I-athsma?

Ewe ☐ Hayi ☐

---

7. Kwiinyanga ezili-12, ezigqithileyo sakha isifuba sakho savakala sishinyene siminxene ngethuba okanye emva komthambo?

Ewe ☐ Hayi ☐

8. Kwiinyanga ezi –12 ezigqithileyo wakha wanalo okhohlokhohlo olomileyo ebusuku,

Ingelulo olomkhuhlane okanye ulosuleleko lwesifuba?

Ewe ☐ Hayi ☐

Yonke imibuzo ibhekiselele xa ungenayo ingqele okanye I-flu **Ewe** **Hayi**

9. Wakha wanayo ingxaki yokuthimla okanye impumlo evuzayo kodwa **Ungenayo** I-flu okanye ingqele? ☐ ☐

Ukuba uphendule "hayi" Nceda tsibela kumbuzo 14

Ewe Hayi

10. Kwezi nyanga zili-12 zigqithileyo, wakha wanengxaki yokuthimla okanye impumlo evuzayo enemfuxane kodwa **Ungenayo I-flu okanye ingqele?** ☐ ☐

Ukuba uphendule "hayi" nceda tsibela kumbuzo 14

Ewe Hayi

11.Kwiinyanga ezili-12, ezigqithileyo, yakha le ngxaki yempumlo yakhatshwa ngamehlo arawuzelayo alilayo/ aneenyembezi? ☐ ☐

12. Yenzeka kuyiphi kwezi nyanga zili-12 zigqithileyo le ngxaki yeempumlo
(Nceda phawula nayiphi elungileyo)

Januari	Februari	Matshi	Apreli
☐	☐	☐	☐
Meyi	**Juni**	**Julayi**	**Agasti**
☐	☐	☐	☐
Septemba	**Oktoba**	**Novemba**	**Decemba**
☐	☐	☐	☐

13. Kwiinynga ezili-12 ezigqithileyo, Ikuphazamise kangakanani le ngxaki yempumlo ukusebenza kwakho kwemihla?

Zange konkel	Kanci nci	gokuphakathi nje	Kakhu lu
☐	☐	☐	☐

Ewe Hayi

14. Wakha wanayo I-hayfever? ☐ ☐

15. Wakha wanayo irashalala erawuzelayo emana ifika iphinde iphele ubuncinane iinyanga ezintandathu ?

Ewe ☐ Hayi ☐

5. Ukuba uphendule "hayi" nceda tsibela kumbuzo 20

---

16. Ukhe wanayo le arshalala irawuzelayo Nanini na kwezi nyanga zili –12 zigqithileyo?

Ewe ☐ Hayi ☐

6. Ukuba uphendule "hayi" nceda Tsibela kumbuzo 20

---

17. Yakha le rashalala irawuzelayo nanini na yakwezindawo zilandelayo?:

Ewe ☐ Hayi ☐

Kwimiphakathi yeengqiniba, emva kwamadolo, ngaphambi kwezihlahla, ezantsi kweempundu, okanye irangqe intamo, iindlebe, namehlo?

18. Yakha yaphela tu le rashalala kwesi sithuba seenyanga ezili 12 Zidlulileyo?

Ewe ☐ Hayi ☐

19. Kwezi nyanga zili-12 ezigqithileyo kukamgaphi ubuncinane,ugcinwa uhleli ebusuku Yile rashalala irhawuzelayo ?

Zange/ kwezi nyangazili-12	Ngaphantsi kobusuku obunye ngeveki	Kanye nangaphezulu ngeveki
☐	☐	☐

---

20. Wakha wanayo I-eczema?

	Ewe	Hayi
	☐	☐

Yima apha.
Nceda yiya uzaliselwe ubunzima nobude bakho phambi kokuba uqhubekeke.

Ubunzima bomzimba: ☐ kg

Ubude: ☐ iiSentimitha

3. Kwezi nyanga zili -12 zigqithileyo, uzitye kangaphi, ubuncinane ezi zidlo zilandelayo?:
(Nceda ushiye kungabhalwanga ukuba akukwazi oko kutya kubuzwayo)

	Zange okanye Nqabileyo	Kanyeokan-ye kabini ngeveki	Kathathu nanga phezulu ngeveki
Inyama(umz. Yenkomo, yegusha, yenkukhu, yehagu)	☐	☐	☐
Ukutya kwasolwandle (kudibanisa nentlanzi)	☐	☐	☐
Iziqhamo	☐	☐	☐
Imifuno/ iiveji (zonke iintlobo)	☐	☐	☐
Ii-erentyisi, iimbotyi	☐	☐	☐
iiCereal (kudibanisa nesonka)	☐	☐	☐
	____	____	____

umbona (uMielie meal, umgubo)	☐	☐	☐
iPasta	☐	☐	☐
IRice	☐	☐	☐
iBhotolo	☐	☐	☐
iMargarine	☐	☐	☐
Amandongomane	☐	☐	☐
ii-tapile	☐	☐	☐
ubisi	☐	☐	☐
amaqanda	☐	☐	☐
Ukutya okukhawulezayo umz. iiburgers	☐	☐	☐

4. Uthamba kangaphi ngeveki okanye uwenza kangaphi umsebenzi onzima ukukwenza uphefumle nzima?:

Zange okanye nqabileyo ☐

Kanye okanye kabini ngeveki ☐

Kathathu nangaphezulu ngeveki ☐

5. Kwiveki eqhelekileyo, zingaphi iiyure obukela kuzo umabona kude?:

Ngaphantsi kwe yure enye ☐

Iyure enye nangaphantsi kweeyure ezi ntathu ☐

Iiyure ezintathu nangaphantsi kweeyure ezintlanu ☐

Iiyure ezi ntlanu nangaphezulu ☐

6. Endlwini kokwenu nisebenzisa esiphi isibasi ngokuqhelekileyo xa niphekayo?:

Umbane ☐

i-Rasi ☐

i-Paraffin ☐

Iinkuni ☐

esinye- nceda cacisa ☐

7. Endlwini, kokwenu nisebenzisa esiphi isibasi ngokuqhelekileyo okwenza shushu?:

Umbane ☐

I-Rasi ☐

i-Paraffin ☐

Iinkuni ☐

Esinye-nceda cacisa ☐

8. Kwezi nyanga zili-12 zigqithileyo uzisele kangaphi ubuncinane, iiPanado?:

Zange ☐

Kanye ngonyaka ubuncinane ☐

Ubuncinane kanye ngenyanga. ☐

9. Bangaphi **abakhuluwa** noodade wenu **abakhulu**?: ☐ Oodade nabakhuluwa

10. Bangaphi **abaninawe** noodade wenu **abancinane**?: ☐ Odade nabaninawe

11. Ingaba wazalelwe e-Kapa?:

Ewe ☐

Hayi ☐

12. Mingaphi iminyaka uhlala e-Kapa?: ☐ Yeminyaka

13. U fike /ugqibe eliphi ibanga lemfundo umama wakho?:

I-Primari skolo ☐

Isikolo samabanga aphezulu (high school) ☐

I-Kholeji, idyunivesiti, okanye olunye uhlobo lwemfundo enomsila ☐

14.Ufike/ ugqibe eliphi ibanga lemfundo utata wakho?:

I- primari skolo ☐

Isikolo samabanga aphezulu (high school) ☐

I-kholeji, idyunivesiti okanye uhlobo lwemfundo enomsila ☐

15. Zigqitha kangaphi ii- truck kwisitrato ohlala kuso kwiintsuku zeveki?

Azigqithi konke konke ☐

Nqabileyo ☐

Qho imini yonke ☐

16. Kwezi nyanga zili-12 zigqithileyo ukhe wanayo ikati ekhayeni lakho?:

Ewe ☐

Hayi ☐

17. Kwezi nyanga zili-12 zigqithileyo ukhe wanayo inja ekhayeni lakho?

Ewe ☐

Hayi ☐

18. Ingaba uyazitshaya iisigarethi umama okanye umgcini wakho obhinqileyo?:

Ewe ☐

Hayi ☐

19. Ingaba uyazitshaya iisigarethi utata wakho okanye umgcini wakho oyindoda?:

Ewe ☐

Hayi ☐

20. Bangaphi abantu abatshaya iisigarethi abahlala endlwini kokwenu ?: ☐ Yabantu

21. Uyazitshaya wena ii-sigarethi?:

Ewe ☐

Hayi ☐

22. Ingaba indlu yenu imanzi okanye ifumile ngaphakathi?:

Ewe ☐

Hayi ☐

23. Ingaba ukho ubani owakha wane TB kusapho lwakowenu?:

Ewe ☐

Hayi ☐

24. Ingaba wena wakha wanyangelwa iTB?:

Ewe ☐

Hayi ☐

25. Bangaphi abantu abahlala endlini yakokwenu?:

Abantu abakhulu ☐

Abantwana ☐

26. Ingaba ninazo Ii- tepu zamanzi abalekayo endlwini yakokwenu?:

Ewe ☐

Hayi ☐

27. Ingaba ninawo umbane indlwini kokwenu?:

Ewe ☐

Hayi ☐

28. Ingaba ninaye umabona-kude (I-TV) endlwini yakokwenu?:

Ewe ☐

Hayi ☐

29. Ingaba unekhaya elinjani?:

Indlu ☐

i-flat ☐

Ityotyombe ☐

Enye Cacisa ☐

30. Ingaba bangaphi abantu abahlala kokwenu abaphangela ngokuqhelekileyo?: ☐ Yabantu

31. Ingaba bangaphi abantu abahlala kokweneu abangaphangeliyo befuna imisebenzi?: ☐ Yabantu

32. Bangaphi abantu ababelana nawe ngegumbi lokulala ebusuku?: ☐ Yabantu

Yima apha linda de kuqaliswe umfanekiso we video phambi kokuphendulaimibuzo elandelayo.

Yima ulinde umfanekiso we-video phambi kokuphendula.

Ewe Hayi

Ukuphefumla kwakho kukhe kwanjena?

Ukuba uthi EWE, ibikhe yenzeka lento kulonyaka ophelileyo?

Ukuba uthi EWE, ibikhe yenzeka kanye okanye kaninzi ngenyanga?

Ewe Hayi

Emva kokuthamba kukhe ukuphefumla kwakho kwafana nokwala nkwenkwe inxibe ihempe **emdaka**, nangaliphi ixesha ebomini bakho?

Ukuba uthi EWE, ibikhe yenzeka lento kulonyaka ophelileyo?

Ukuba uthiEWE, ibikhe yenzeka kanye okanye kaninzi ngenyanga?

Ewe Hayi

Wakha wavuka unjena ebusuku, nangaliphi ixesha ebomini bakho?

Ukuba kunjalo, ibikhe yenzeka lento kulonyaka ophelileyo?

Ukuba kunjalo, ibikhe yenzeka kanye okanye kaninzi ngenyanga?

Ewe Hayi

Wakha wavuka unjena ebusuku?

Ukuba kunjalo, ibikhe yenzeka lento kulonyaka ophelileyo?

Ukuba kunjalo, ibikhe yenzeka kanye okanye kaninzi ngenyanga?

Ewe Hayi

Wakhe waphefumla kanjena, nangaliphi ixesha ebomini bakho?

Ukuba uthi EWE, ibikhe yenzeka lento kulonyaka ophelileyo?

Ukuba kunjalo, ibikhe yenzeka kanye okanye kaninzi ngenyanga?

Appendix 1G: Questionnaire (Afrikaans version)

OPNAME VAN ASEMHALINGS, NEUS EN VELPROBLEME

Alleenlik vir kantoorgebruik | | | | | | | | |

VII. Aanwysings vir die voltooing van die vraelys

Hierdie vraelys bevat vrae met betrekking tot jou naam, adres en geboortedatum. Skryf asseblief jou antwoorde neer in die spasies voorsien.

Al die ander vrae moet beantwoord word deur 'n merkie in die blokkie te maak wat jy kiesof die antwoord in die blokkie te skryf. Indien jy jou antwoord wil verander, trek net 'n kruisie deur die blokkie en merk dan die regte een**. Merk slegs een blokkie per vraag**.

Hier is n voorbeeld: Ouderdom ☐ jaar

	Ja	Nee
Om ja of nee te antwoord, plaas net 'n merkie		
In die ooreenstemmende blokkie	☐	☐

Naam:

Skool:

Huisadres:

Vandag se datum: ☐☐ ☐☐ ☐☐

Dag Maand Jaar

Jou ouderdom: ☐☐

Jaar

Jou geboortedatum: ☐☐ ☐☐ ☐☐

Dag Maand Jaar

Jou geslag: ☐ ☐

Seun Meisie

Is jy in Kaapstad gebore? Ja ☐ Nee ☐

Indien jy nie in Kaapstad gebore is nie, op watter ouderdom het jy hierheen verhuis? ☐☐

Jaar

1. Het jy al ooit 'n fluit of hygbors gehad?

	Ja	Nee

7. INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 6

---

2. Het jy 'n fluit of hygbors gedurende die afgelope 12 maande gehad?

Ja	Nee

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 6

---

3. Hoeveel aanvalle van fluit of hygbors het jy in die afgelope 12 maande gehad?

Geen	1 tot 3	4 tot 12	Meer as 12

4. In die afgelope 12 maande, hoeveel keer is jou slaap daardeur bederf?

Nooit as gevolg van fluit/hygbors wakker geword nie	Minder as 1 keer per week	1 of meer nagte per week

5. Was die fluit of hygbors ooit so erg die afgelope 12 maande, dat jy slegs 1 of 2 woorde per asemtog kon praat?

Ja	Nee

6.. Het jy al ooit asma gehad?

Ja	Nee

---

7. Het jou bors in die afgelope 12 maande gefluit gedurende of na oefening?

Ja	Nee

14. Het jy gedurende die afgelope 12 maande ooit 'n droë hoes gedurende die nag ervaar buiten wanneer jy 'n verkoue of griep gehad het?

Ja	Nee

DIE VOLGENDE VRAE HANDEL OOR SIMPTOME WAT JY ERVAAR HET, MAAR NIE TEN TYE VAN 'N VERKOUE OF GRIEP NIE.

	Ja	Nee
9. Het jy al ooit 'n probleem met 'n geniesery, loop of toeneus gehad, buiten wanner jy verkoue of griep gehad het?	☐	☐

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 14

	Ja	Nee
10. Het jy in die afgelope 12 maande probleme met 'n geniesery, loop of toeneus gehad, wanneer jy nie verkoue of griep gehad het nie?	☐	☐

INDIEN JY "NEE" GEANWOORD HET, GAAN DIREK NA VRAAG 14

	Ja	Nee
11. Het jou neusprobleem in die afgelope 12 maande gepaard gegaan met jeukerige/tranerige oë	☐	☐

15. Gedurende watter van die afgelope 12 maande het jou neusprobleme geduur?
(Dui asseblief almal aan wat van toepassing is)

Januarie ☐	Februarie ☐	Maart ☐	April ☐
Mei ☐	Junie ☐	Julie ☐	Augustus ☐
September ☐	Oktober ☐	November ☐	Desember ☐

13. Hoe dikwels het jou neusprobleme in die afgelope 12 maande jou daaglikse aktiwiteite beïnvloed

Glad nie ☐	Effens ☐	Taamlik baie ☐	Baie ☐

	Ja	Nee
16. Het jy al ooit hooikoors gehad?	☐	☐

15. Het jy al ooit 'n jeukerige veluitslag gehad wat gekom gaan het oor tenminste 6 maande?

Ja	Nee
☐	☐

8. INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 20

---

17. Het jy hierdie jeukerige uitslag die afgelope 12 maande gehad?

Ja	Nee
☐	☐

9. INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 20

---

17. Het hierdie jeukerige uitslag enige van die volgende areas aangetas?:

Die elmboë se voue, agter die knieë, aan die voorkant van die enkels, onder die boude, om die nek, ore of oë?

Ja	Nee
☐	☐

18. Het hierdie uitslag ooit gedurende die afgelope 12 maande totaal opgeklaar?

Ja	Nee
☐	☐

19. Hoe gereeld het die jeukerige uitslag jou gedurende die afgelope 12 maande snags wakker gehou?

Nooit in die afgelope 12 maande nie	Minder as 1 keer per week	1 of meer keer per week
☐	☐	☐

---

20. Het jy al ooit ekseem gehad?

Ja	Nee
☐	☐

STOP HIER.

LAAT NEEM JOU MASSA EN LENGTE VOORDAT JY VERDER GAAN

9. Massa: ☐ kg

10. Lengte: ☐ cm

11. Gedurende die afgelope 12 maande, hoe dikwels het jy die volgende geëet of drink? (Laat asseblief 'n spasie indien jy nie die voedselsoort ken nie)

	Nooit of af en toe	Een of tweekeer per week	Drie of meerkeer per week
Vleis (bv. Bees, lam, hoender, vark)	☐	☐	☐
Seekos (insluitend vis)	☐	☐	☐
Vrugte	☐	☐	☐
Groente (alle soorte)	☐	☐	☐
Erte, bone	☐	☐	☐
Graankos (insluitend brood)	☐	☐	☐
Mielies (mieliemeel)	☐	☐	☐
Pasta	☐	☐	☐
Rys	☐	☐	☐

Botter	☐	☐	☐
Margarien	☐	☐	☐
Neute (insluitend grondbone)	☐	☐	☐
Aartappels	☐	☐	☐
Melk	☐	☐	☐
Eiers	☐	☐	☐
Kitskos/Burgers	☐	☐	☐

12. Hoeveel keer per week doen jy oefeninge of fisiese arbeid wat jou hard laat asemhaal?

Nooit of soms ☐

Een of tweekeer per week ☐

Drie of meerkeer per week ☐

13. Gedurende ’n normale week, hoeveel uur **<u>per dag</u>** kyk jy televisie?:

Minder as ’n uur ☐

1 uur of meer, maar minder as 3 ure ☐

3 ure of meer, maar minder as 5 ure ☐

5 ure of meer ☐

14. Watter tipe brandstof word in jou huis gebruik vir koskook?:

Elektrisiteit ☐

Gas ☐

Paraffien ☐

Hout (insluitend oop vure) ☐

Ander – spesifiseer asseblief ☐

15. Watter tipe brandstof word in jou huis gebruik vir verhitting?:

Elektrisiteit ☐

Gas ☐

Paraffien ☐

Hout (insluitend oop vure) ☐

Ander – spesifiseer asseblief ☐

16. Hoeveel keer gedurende die afgelope 12 maande het jy Panado gedrink?:

Nooit ☐

Ten minste 1 keer per jaar ☐

Ten minste 1 keer per maand ☐

9. Hoeveel **ouer** broers en susters het jy? ☐ Broers en susters

10. Hoeveel **jonger** broers en susters het jy? ☐ Broers en susters

18. Is jy in Suid Afrika gebore?:

Ja ☐

Nee ☐

12. Hoeveel lank woon jy al in Suid Afrika?: ☐ jaar

19. Watter vlak van opleiding het jou moeder bereik or voltooi?:

Primêre skool ☐

Hoër skool ☐

Kollege, universiteit of ander vorm van tersiëre opleiding ☐

20. Watter vlak van opleiding het jou vader bereik of voltooi?:

Primêre skool ☐

Hoër skool ☐

Kollege, universiteit of enige ander vorm van tersiëre opleiding ☐

21. Hoe dikwels ry vragmotors in die straat af waar jy woon?:

Nooit ☐

Selde ☐

Gereeld gedurende die dag ☐

16 Het julle die afgelope 12 maande 'n kat in die huis gehad?:

Ja ☐

Nee ☐

17. Het julle die afgelope 12 maande 'n hond in die huis gehad?:

Ja ☐

Nee ☐

18. Rook jou moeder (of die vroulike persoon wat na jou kyk) sigarette?:

Ja ☐

Nee ☐

19. Rook jou vader (of die manlike persoon wat na jou kyk) sigarette?:

Ja ☐

Nee ☐

20. Hoeveel inwoners van jou huis, rook sigarette ☐ inwoners

21. Rook jy sigarette?:

Ja ☐

Nee ☐

22. Is jou huis aan die binnekant, klam of nat?:

Ja ☐

Nee ☐

23. Het enige een in jou huis al ooit TB gehad?:

Ja ☐

Nee ☐

24. Is jy al ooit vir TB behandel?:

Ja ☐

Nee ☐

25. Hoeveel mense woon in jou huis?:

Volwassenes ☐

Kinders ☐

26. Is daar krane met lopende water in jou huis?:

Ja ☐

Nee ☐

27. Is daar elektrisiteit in jou huis?:

Ja ☐

Nee ☐

28. Is daar ’n TV in jou huis?:

Ja ☐

Nee ☐

29. Waarin woon jy?:

Huis ☐

Woonstel ☐

Hut ☐

Ander ☐

30. Hoeveel inwoners van jou huis het ’n vaste betrekking?: ☐ inwoners

31. Hoeveel inwoners van jou huis is werkloos of opsoek na werk?: ☐ inwoners

32. Met hoeveel mense deel jy ’n kamer gedurende die nag?: ☐ mense

STOP HIER.

WAG VIR DIE VIDEO OM TE BEGIN VOORDAT JY DIE RES VAN DIE VRAELYS VOLTOOI

	Ja	Nee
1. Was jou asemhaling al soos dié?:		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
2. Was jou asemhaling al ooit soos die van die seun met die **donker** hemp na oefening?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
3. Het jy ooit in jou lewe snags so wakker geskrik?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
4. Het jy al ooit soos dié gedurende die nag wakker geword?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
5. Was jou asemhaling al ooit soos dié?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

Appendix II: Online Repository Materials

Table i: Prevalence estimates of all sociodemographic variables

Variable	Responses (N=5,037)	Percentage (%)
Medium of instruction at school		
Afrikaans	1,289	25.59
English	2,059	40.88
Xhosa	1,689	33.53
Age		
≤13 years	2,604	51.70
≥14 years	2,432	48.28
Gender		
Male	2, 026	40.20
Female	2, 995	59.5
Invalid	16	0.32
Cape Town city of birth		
Yes	4, 074	80.88
No	934	18.54
Invalid	29	0.58
What level of education has your mother reached or completed?		

Variable	Responses (N=5,037)	Percentage (%)
Primary school	922	18.30
High school	2, 960	58.77
College, university or other form of tertiary education	1, 086	21.56
What level of education has your father reached or completed?		
Primary school	865	17.17
High school	2, 571	51.04
College, university or other form of tertiary education	1, 313	26.07
≥4	1, 541	30.59
Invalid	456	9.05
Do you have a TV in your house?		
Yes	4, 504	89.42
No	346	6.87
No response	187	3.71
How many people in your household are working?		
0	289	5.74
1	1, 549	30.75

Variable	Responses (N=5,037)	Percentage (%)
2	1, 707	33.89
3	598	11.87
≥4	352	6.99
Invalid	542	10.76
How many people in your household are not working?		
0	1, 652	32.80
1	1, 507	29.92
2	724	14.37
3	251	4.98
≥4	150	2.98
Invalid	753	14.95

Table ii: Prevalence estimates of all diet variables

Diet in past 12 months	Never or rarely (%)	Once or twice per week (%)	Three or more times a week (%)	Missing (%)
Meat	339 (6.73)	2, 095 (41.59)	2, 431 (48.26)	172 (3.41)
Seafood	2, 174 (43.16)	2, 184 (43.36)	391 (7.76)	288 (5.72)
Fruit	335 (6.65)	1, 421 (28.21)	3, 092 (61.39)	189 (3.75)
Vegetables	613 (12.17)	1, 648 (32.72)	2, 549 (50.61)	227 (4.51)
Peas, beans	1, 561 (30.99)	2, 274 (45.15)	929 (18.44)	273 (5.42)
Cereal	459 (9.11)	842 (16.72)	3, 438 (68.25)	298 (5.92)
Maize	2, 224 (44.15)	1, 651 (32.78)	879 (17.45)	283 (5.62)
Pasta	1, 332 (26.44)	2, 434 (48.32)	827 (16.42)	444 (8.81)
Rice	253 (5.02)	1, 155 (22.93)	3, 445 (68.39)	184 (3.65)
Butter	916 (18.19)	1, 125 (22.33)	2, 710 (53.80)	286 (5.68)

Margarine	1, 267 (25.15)	1, 384 (27.48)	1, 979 (39.29)	407 (8.08)
Nuts	1, 951 (38.73)	1, 976 (39.23)	833 (16.54)	277 (5.50)
Potatoes	203 (4.03)	1, 292 (25.65)	3, 339 (66.29)	203 (4.03)
Milk	444 (8.81)	1, 317 (26.15)	3, 065 (60.85)	211 (4.19)
Eggs	672 (13.34)	2, 530 (50.23)	1, 588 (31.53)	247 (4.90)
Fast food/burgers	980 (19.46)	2, 384 (47.33)	1, 326 (26.33)	347 (6.89)

Table iii: Prevalence estimates of all other environmental exposures

How many times a week do you have enough exercise or physical effort to make you breathe hard?		
Never or occasionally	1, 572	31.21
Once or twice per week	2, 103	41.75
Three or more times a week	1, 181	23.45
Missing	181	3.59
During a normal week, how many hours a day do you watch television?		
Less than 1 hour	563	11.18
1 hour but less than 3 hours	1, 303	25.87
3 hours but less than 5 hours	1, 353	26.86
5 hours or more	1, 620	32.16
In your house, what fuel is usually used for cooking?		
Electricity	4, 436	88.07
Gas	503	9.99
Paraffin	892	17.71
Wood	83	1.65
Other	1	0.02
In your house, what fuel is usually used for heating?		

Electricity	3, 540	70.28
Gas	231	4.59
Paraffin	1, 177	23.37
Wood	303	6.02
Other	19	0.38
In the past 12 months, how often, on average, have you taken Panado?		
Never	1, 333	26. 46
At least once a year	1, 764	35.02
At least once per month	1, 741	34.56
Missing	199	3.95
How often do trucks pass along the street where you live, on weekdays?		
Never	582	11.55
Seldom	2, 249	44.65
Frequently during the day	2, 015	40.00
Missing	191	3.79
In the past 12 months, have you had a cat in your home?		
Yes	1, 526	30.30
No	3, 337	66.25

No response	174	3.45
In the past 12 months, have you had a dog in your home?		
Yes	2, 663	52.87
No	2, 192	43.52
No response	182	3.61
Does your mother (or female care giver) smoke cigarettes?		
Yes	1, 405	27.89
No	3, 419	67.88
No response	213	4.23
Does your father (or male care giver) smoke cigarettes?		
Yes	2, 130	42.29
No	2, 626	52.13
No response	281	5.58
Do you smoke cigarettes?		
Yes	433	8.60
No	4, 417	87.69
No response	187	3.71
Has anyone in your household ever had TB?		

Yes	691	13.72
No	4, 133	82.05
No response	213	4.23
Have you ever been treated for TB?		
Yes	325	6.45
No	4, 447	88.29
No response	265	5.26
How many older brothers and sisters do you have?		
0	900	17.87
1	1, 371	27.22
2	933	18.52
3	544	10.80
≥4	500	9.93
Invalid	789	15.66
How many younger brothers and sisters do you have?		
0	986	19.58
1	1, 737	34.48
2	977	19.40

3	358	7.11
≥4	190	3.77
Invalid	789	15.66
How many people living in your house smoke cigarettes?		
0	1, 399	27.77
1	1, 308	25.97
2	901	17.89
3	429	8.52
≥4	447	8.87
Invalid	553	10.98
How many adults live in your household?		
1	425	8.44
2	2, 263	44.93
3	823	16.34
≥4	1, 101	21.86
Invalid	425	8.44
How many children live in your household?		
1	509	10.11

2	1, 298	25.77
3	1, 233	24.48
Is your house damp or wet inside?		
Yes	507	10.07
No	4, 305	85.47
No response	225	4.47
Do you have taps for running water in your house?		
Yes	3, 861	76.65
No	933	18.52
No response	243	4.82
Do you have electricity in your house?		
Yes	4, 666	92.63
No	181	3.59
No response	190	3.77
What type of home do you have?		
House	3, 936	78.14
Flat	263	5.22
Shack	573	11.38

Other	60	1.19
Missing	205	4.07
How many people share your bedroom at night?		
0	1, 201	23.84
1	1, 285	25.51
2	1, 078	21.40
3	544	10.80
≥4	417	8.28
Invalid	512	10.16

Table iv: Bivariate analysis: allergic rhinitis, atopic eczema and comorbid symptoms with remaining sociodemographic and environmental exposures

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
Age															
≤13 years	530	2, 604	0.96	0.83-1.11	0.60	342	2, 604	1.07	0.90-1.27	0.46	121	2, 604	0.93	0.72-1.20	0.57
≥14 years	513	2, 433	1.00			327	2, 433	1.00			123	2, 433	1.00		
What level of education has your father reached or completed?															
Primary school	201	865	1.05	0.87-1.27	0.59	127	865	1.05	0.83-1.31	0.70	51	865	1.19	0.86-1.63	0.29
Secondary school	537	2, 571	1.03	0.89-1.19	0.69	327	2, 571	0.82	0.69-0.98	0.03	124	2, 571	1.00	0.77-1.29	0.99
Tertiary education	276	1, 313	1.03	0.87-1.22	0.71	162	1, 313	1.06	0.86-1.30	0.57	56	1, 313	0.86	0.63-1.17	0.33
How many adults live in your household?															

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
0-1	99	425	1.00			71	425	1.00			23	425	1.00		
2	473	2, 263	0.81	0.62-1.06	0.13	270	2, 263	0.70	0.51-0.96	0.03	99	2, 263	0.82	0.51-1.31	0.41
3	164	823	0.72	0.53-0.98	0.04	108	823	0.74	0.51-1.05	0.09	41	823	0.89	0.53-1.51	0.67
≥4	233	1, 101	0.82	0.61-1.10	0.18	173	1, 101	0.90	0.64-1.27	0.54	61	1, 101	1.01	0.61-1.66	0.98
Missing	425					425					425				
How many children live in your household?															
0-1	123	509	1.00			71	509	1.00			34	509	1.00		
2	269	1, 298	0.80	0.61-1.04	0.10	149	1, 298	0.82	0.59-1.14	0.24	49	1, 298	0.55	0.35-0.87	0.01

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
3	276	1, 233	0.89	0.68-1.16	0.38	158	1, 233	0.79	0.57-1.10	0.17	62	1, 233	0.73	0.47-1.13	0.15
≥4	295	1, 541	0.71	0.55-0.93	0.01	237	1, 541	0.96	0.70-1.31	0.80	75	1, 541	0.69	0.45-1.06	0.09
Missing	456					456					456				
How many times a week do you have enough exercise or physical effort to make you breathe hard?															
Never or occasionally	310	1, 572	1.00			197	1, 572	1.00			67	1, 572	1.00		
Once or twice per week	456	2, 103	1.19	1.00-1.42	0.05	299	2, 103	1.27	1.03-1.56	0.03	126	2, 103	1.46	1.08-1.99	0.02
Three or more times a week	248	1, 181	1.18	0.96-1.44	0.11	158	1, 181	1.24	0.97-1.58	0.09	46	1, 181	0.93	0.64-1.37	0.73
Missing	181					181					181				
During a normal week, how many hours a **day** do you watch television?															

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
Less than 1 hour	108	563	1.00			78	563	1.00			35	563	1.00		
1 hour but less than 3 hours	272	1, 303	1.12	0.86-1.46	0.42	167	1, 303	0.94	0.69-1.29	0.71	58	1, 303	0.70	0.45-1.08	0.11
3 hours but less than 5 hours	297	1, 353	1.19	0.91-1.54	0.20	175	1, 353	0.97	0.71-1.32	0.86	72	1, 353	0.84	0.55-1.27	0.41
5 hours or more	342	1, 620	1.21	0.94-1.57	0.15	228	1, 620	0.98	0.73-1.32	0.91	75	1, 620	0.74	0.49-1.13	0.16
Missing	198					198					198				
Were you born in South Africa?															
Yes	888	4, 172	1.02	0.81-1.29	0.87	535	4, 172	0.62	0.48-0.79	0.00	207	4, 172	0.99	0.67-1.45	0.96
No	116	682	1.00			121	682	1.00			32	682	1.00		
No response	183					183					183				
How often do trucks pass along the street where you live, on weekdays?															
Never	119	582	1.00			79	582	1.00			35	582	1.00		
Seldom	461	2, 249	1.04	0.82-1.33	0.72	273	2, 249	0.90	0.67-1.20	0.47	100	2, 249	0.74	0.50-1.11	0.14

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
Frequently during the day	434	2, 015	1.08	0.85-1.38	0.51	295	2, 015	1.00	0.74-1.33	0.98	104	2, 015	0.84	0.56-1.25	0.39
Missing	191					191					191				
In the past 12 months, have you had a cat in your home?															
Yes	333	1, 526	0.98	0.83-1.15	0.78	210	1, 526	1.00	0.83-1.21	0.99	81	1, 526	1.09	0.82-1.43	0.56
No	680	3, 337	1.00			444	3, 337	1.00			156	3, 337	1.00		
No response	174					174					174				
In the past 12 months, have you had a dog in your home?															
Yes	571	2, 663	1.06	0.91-1.22	0.48	363	2, 663	0.98	0.82-1.17	0.82	138	2, 663	1.13	0.87-1.48	0.36
No	446	2, 192	1.00			288	2, 192	1.00			100	2, 192	1.00		
No response	182					182					182				
Does your father (or male care giver) smoke cigarettes?															
Yes	473	2, 130	1.07	0.92-1.25	0.36	297	2, 130	0.99	0.82-1.18	0.89	125	2, 130	1.36	1.04-1.78	0.02
No	520	2, 626	1.00			340	2, 626	1.00			111	2, 626	1.00		
No response	281					281					281				
How many older brothers and sisters do you have?															

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
0	192	900	1.00			144	900	1.00			45	900	1.00		
1	296	1, 371	0.92	0.73-1.15	0.44	189	1, 371	0.75	0.58-0.97	0.03	71	1, 371	1.01	0.69-1.49	0.95
2	172	933	0.74	0.58-0.95	0.02	107	933	0.58	0.43-0.78	0.00	35	933	0.71	0.45-1.12	0.15
3	123	544	1.02	0.77-1.34	0.93	75	544	0.77	0.55-1.07	0.12	35	544	1.32	0.84-2.10	0.23
≥4	103	500	0.90	0.67-1.21	0.50	83	500	0.90	0.65-1.25	0.53	29	500	1.15	0.71-1.86	0.58
Missing	789					789					789				
How many younger brothers and sisters do you have?															
0	209	986	1.00			134	986	1.00			49	986	1.00		
1	369	1, 737	0.86	0.70-1.06	0.16	230	1, 737	0.92	0.72-1.18	0.52	81	1, 737	0.90	0.62-1.30	0.57
2	180	977	0.75	0.59-0.96	0.02	157	977	1.06	0.81-1.39	0.67	50	977	0.98	0.65-1.47	0.91
3	73	358	0.88	0.64-1.22	0.45	50	358	0.90	0.61-1.32	0.58	20	358	1.12	0.65-1.93	0.68
≥4	43	190	1.04	0.69-1.56	0.85	36	190	1.15	1.74-1.80	0.53	10	190	0.96	0.48-1.95	0.92
Missing	789					789					789				
How many people living in your house smoke cigarettes?															
0	271	1, 399	1.00			179	1, 399	1.00			50	1, 399	1.00		

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**	**n**	**N=5, 037**	**OR**	**95% CI**	**p-value**
1	263	1, 308	0.91	0.74-1.11	0.36	195	1, 308	1.03	0.81-1.31	0.83	65	1, 308	1.32	0.91-1.93	0.15
2	178	901	0.81	0.65-1.02	0.07	108	901	0.72	0.55-0.95	0.02	42	901	1.21	0.79-1.84	0.38
3	108	429	1.18	0.90-1.57	0.23	56	429	0.72	0.51-1.02	0.07	26	429	1.57	0.96-2.56	0.07
≥4	117	447	1.07	0.82-1.39	0.63	57	447	0.66	0.47-0.93	0.02	31	447	1.73	1.09-2.75	0.02
Missing	553					553					553				

Table v: Bivariate analysis: allergic rhinitis, atopic eczema and comorbid symptoms with remaining dietary exposures

	Allergic Rhinitis					Atopic Eczema					Allergic Rhinitis and Atopic Eczema				
Exposure	**n**	**N=5,037**	**OR**	**95% CI**	**p - value**	**n**	**N=5,037**	**OR**	**95% CI**	**p - value**	**n**	**N=5,037**	**OR**	**95% CI**	**p - value**
Meat-1	72	339	1.00			53	339	1.00			25	339	1.00		
Meat-2	416	2, 095	0.89	0.65-1.20	0.43	259	2, 095	0.89	0.63-1.26	0.52	87	2, 095	0.55	0.35-0.88	0.01
Meat-3	529	2, 431	1.08	0.80-1.47	0.60	337	2, 431	0.99	0.71-1.39	0.97	125	2, 431	0.71	0.45-1.11	0.13
Meat-9	172					172					172				
Seafood-1	455	2, 174	1.00			263	2, 174	1.00			107	2, 174	1.00		
Seafood -2	450	2, 184	1.00	0.85-1.17	0.99	308	2, 184	1.20	0.99-1.45	0.06	107	2, 184	1.02	0.77-1.34	0.91
Seafood -3	93	391	1.17	0.89-1.54	0.26	63	391	1.10	0.80-1.51	0.58	19	391	0.90	0.54-1.49	0.68
Seafood -9	288					288					288				
Fruit-1	82	335	1.00			44	335	1.00			18	335	1.00		
Fruit-2	291	1, 421	0.73	0.54-0.99	0.05	183	1, 421	0.98	0.67-1.43	0.90	67	1, 421	0.88	0.51-1.50	0.63
Fruit-3	641	3, 092	0.75	0.56-1.01	0.06	414	3, 092	1.03	0.72-1.48	0.88	150	3, 092	0.90	0.54-1.50	0.69

Fruit-9	189					189					189				
Maize-1	504	2, 224	1.00			237	2, 224	1.00			84	2, 224	1.00		
Maize -2	297	1, 651	0.79	0.67-0.94	0.01	231	1, 651	1.35	1.09-1.66	0.01	84	1, 651	1.39	1.02-1.90	0.04
Maize -3	190	879	1.02	0.83-1.26	0.84	163	879	1.79	1.41-2.27	0.00	61	879	1.86	1.32-2.62	0.00
Maize -9	283					283					283				
Pasta-1	257	1, 332	1.00			208	1, 332	1.00			66	1, 332	1.00		
Pasta -2	537	2, 434	1.04	0.87-1.24	0.64	283	2, 434	0.69	0.56-0.86	0.01	110	2, 434	0.89	0.65-1.22	0.49
Pasta -3	181	827	0.98	0.78-1.23	0.85	120	827	0.72	0.55-0.94	0.02	52	827	1.19	1.82-1.74	0.36
Pasta -9	444					444					444				
Rice-1	51	253	1.00			45	253	1.00			18	253	1.00		
Rice-2	211	1, 155	0.99	0.69-1.41	0.94	128	1, 155	0.70	0.46-1.05	0.08	48	1, 155	0.65	0.37-1.14	0.13
Rice-3	745	3, 445	1.25	0.89-1.75	0.19	463	3, 445	0.77	0.53-1.11	0.16	169	3, 445	0.75	0.45-1.24	0.26
Rice-9	184					184					184				
Butter-1	176	916	1.00			116	916	1.00			37	916	1.00		

Butter-2	206	1, 125	0.90	0.71-1.15	0.41	163	1, 125	1.11	0.84-1.47	0.46	56	1, 125	1.24	0.81-1.91	0.32
Butter- 3	599	2, 710	1.10	0.90-1.35	0.36	341	2, 710	0.90	0.70-1.14	0.39	131	2, 710	1.19	0.81-1.73	0.37
Butter-9	286					286					286				
Margarine-1	262	1, 267	1.00			145	1, 267	1.00			58	1, 267	1.00		
Margarine-2	272	1, 384	0.96	0.79-1.18	0.71	195	1, 384	1.30	1.01-1.65	0.05	69	1, 384	1.10	0.76-1.57	0.62
Margarine-3	431	1, 979	1.13	0.94-1.36	0.20	272	1, 979	1.26	1.00-1.59	0.05	101	1, 979	1.12	0.80-1.56	0.51
Margarine-9	407					407					407				
Nuts-1	396	1, 951	1.00			239	1, 951	1.00			94	1, 951	1.00		
Nuts-2	411	1, 976	1.05	0.89-1.24	0.53	252	1, 976	0.98	0.80-1.21	0.89	85	1, 976	0.89	0.66-1.21	0.47
Nuts- 3	177	833	1.09	0.88-1.35	0.45	132	833	1.15	0.89-1.47	0.28	48	833	1.16	0.81-1.67	0.41
Nuts-9	277					277					277				
Potatoes-1	37	203	1.00			29	203	1.00			9	203	1.00		
Potatoes-2	252	1, 292	1.28	0.75-1.69	0.56	158	1, 292	1.01	0.64-1.60	0.95	47	1, 292	0.88	0.42-1.83	0.73

Potatoes-3	714	3, 339	1.28	0.87-1.89	0.21	445	3, 339	1.05	0.68-1.63	0.81	177	3, 339	1.29	0.65-2.57	0.47
Potatoes-9	203					203					203				
Milk-1	95	444	1.00			71	444	1.00			26	444	1.00		
Milk-2	241	1, 317	0.89	0.67-1.19	0.43	193	1, 317	0.96	0.69-1.32	0.80	59	1, 317	0.80	0.49-1.29	0.36
Milk- 3	671	3, 065	1.00	0.77-1.29	0.97	375	3, 065	0.80	0.56-0.93	0.15	150	3, 065	0.86	0.56-1.33	0.51
Milk-9	211					211					211				
Eggs-1	144	672	1.00			90	672		1.00		34	672	1.00		
Eggs-2	517	2, 530	0.95	0.76-1.19	0.65	280	2, 530	0.80	0.61-1.06	0.11	101	2, 530	0.80	0.54-1.19	0.28
Eggs- 3	337	1, 588	1.09	0.86-1.38	0.48	258	1, 588	1.20	0.91-1.60	0.20	96	1, 588	1.24	0.83-1.87	0.29
Eggs-9	247					247					247				
Fastfood-1	181	980	1.00			122	980	1.00			42	980	1.00		
Fastfood-2	497	2, 384	1.12	0.91-1.37	0.27	284	2, 384	0.87	0.68-1.11	0.26	110	2, 384	1.08	0.75-1.55	0.70
Fastfood- 3	305	1, 326	1.15	0.92-1.43	0.23	207	1, 326	1.00	0.77-1.30	0.99	73	1, 326	1.18	0.80-1.75	0.40
Fastfood-9	347					347					347				